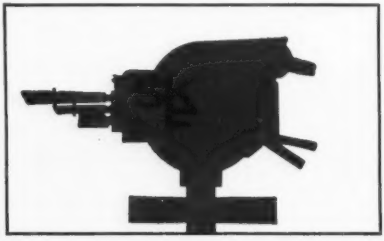
consultant

November 1961

From SK&F—to help you in your practice



Medical Color Television—*one of the many services offered to physicians by SK&F*

SK&F's Color Television gives physicians otherwise unobtainable close-up views of surgical and clinical procedures. An average of 55,000 doctors a year see these "live," full-color programs at postgraduate medical meetings. Other services to you include:

- SK&F Medical Films
- Special Resin No. 648 for the control of hyperkalemia in renal insufficiency
- Product overdosage information
- Mental Health Services

For a copy of our medical film catalogue, supplies of our products, or information about other services, ask your SK&F representative, write Smith Kline & French Laboratories, 1500 Spring Garden Street, Philadelphia 1, Penna., or call us at LOcust 4-2400.

consultant

November 1961

CONSULTANT is published monthly by Smith Kline & French Laboratories for practicing physicians. Authors are chosen because of expert knowledge of their topics, and their participation does not imply endorsement of any of the products advertised. As a service to readers, the authors will answer questions pertaining to their topics; the most informative questions and answers will be published in later issues. CONSULTANT welcomes original manuscripts and suggestions for topics. Please address all correspondence, including questions for the authors, to CONSULTANT, Smith Kline & French Laboratories, 1500 Spring Garden St., Philadelphia 1, Pa.

CORRESPONDENCE

CONSULTANT welcomes questions and comments about any of the topics covered. The authors will answer all questions by mail, and some of the most informative replies will be published in this section (names will be withheld on request). Please address all correspondence to CONSULTANT, SK&F Laboratories, 1500 Spring Garden Street, Philadelphia 1, Pa.

Treatment of Lacerations in Children

(CONSULTANT, July '61)

Dear Doctor Metzger:

. . . We gently clean with Bactine®, then use 2 to 10 cc. of 2% procaine HCl in saline via 24-gauge needle injected under the skin through the laceration. Usually we use 3-0 or 4-0 silk on atraumatic needles for skin. If subcutaneous sutures are needed, we use 3-0 plain catgut.

No hoots nor hollers nor holds when the sutures are removed because it didn't hurt to get them put in.

—Charles C. Reher, M.D.
Clinton, Pa.

The Need for Investigating Glycosuria

(CONSULTANT, June '61)

Dear Doctor Lee:

I enjoyed very much your article in the June issue of "Consultant" entitled "Diabetes—A Plea for Early Treatment."

The article was especially interesting to me because I perform the yearly management physical examinations at the National Tube Division, Lorain Works, U.S. Steel Corporation. Frequently a trace of sugar is found in a routine urine examination, but often the repeat examination is negative. Because of this, I have found it hard to convince many of the men that regular post-prandial blood sugar determinations should be made. These men are all referred to their family physicians, but unfortunately many of these physicians are also of the opinion that a little sugar now and then is of no importance.

I am enclosing a copy of a condensation I made of your article, and would like your permission to send it to all the patients with glycosuria and also to those who have a family history of diabetes. I think that the patient and perhaps also his family doctor will in this way be persuaded to regard the "trace" more seriously.

—E. S. Ball, M.D.
Lorain, Ohio

I am flattered by your letter concerning the article on diabetes in CONSULTANT. I think your abstract is entirely satisfactory and I have no objection to your giving it to any employees who are found to have glycosuria or to their doctors. I would certainly think that you might include it in any report that you send the family doctor of any employee who is found to have glycosuria. Whether your steel workers will be interested in it, I will leave up to you. If some of them are and, in turn, will stimulate their own doctors to be a bit more thorough, we will have accomplished something worthwhile – even if by the back door.

– Charles T. Lee, Jr., M.D.

Management of Idiopathic Hypoglycemia

Sir:

Please suggest a diet to be given for a seven-year-old child who has clinical and laboratory evidence of idiopathic hypoglycemia. A sibling of three months has definitely been found to have leucine hypoglycemia. What is the best source of protein and which proteins are lowest in leucine?

– Henry C. Petersen, M.D.
Stockton, California

The two siblings you describe with familial hypoglycemia are interesting. Our usual diet for the seven-year-old would include a regimen of three small meals plus a high-carbohydrate, high-fat feeding, such as ice cream with milk, between feedings and at bedtime. Our basic low-leucine diet is essentially a low-protein diet. Fortunately, several milk companies now make formulas for infants containing 1.5% protein. We have not found any easily available proteins sufficiently deficient in leucine but the low-protein formula is adequate for growth and frequently minimizes symptoms, especially if added carbohydrate and fat feedings are interspersed. If the children's symptoms are not controlled on diet alone, we use ACTH or cortisone to raise the blood sugar. Many children with hypoglycemia can be controlled with these agents. If they are not, we next consider partial pancreatectomy.

– Lewis A. Barness, M.D.

A Compliment and a Request

Sir:

First, congratulations on the new medical journal CONSULTANT. The calibre of your articles is outstanding for clarity and usefulness in the everyday practice of medicine. Double the congratulations for the separating of the articles by an advertising page so that removal of a complete article can be accomplished for filing for future use. Sincerely hope other journals will see the advantage of this format.

I missed out on receiving the June number and would appreciate receiving a copy of the chart regarding medical ineligibility to drive a motor vehicle.

—L. Huntley Cate, M.D.
Brightwood, Virginia

Our thanks to Dr. Cate for his praise. We truly appreciate receiving opinions from readers—pro and con—and especially welcome suggestions for articles that would help solve difficult clinical problems. Copies of back issues of CONSULTANT are still available, and so are the free materials offered, such as the chart listing medical conditions which may make persons ineligible for driving.—ED.

ORTHOPEDICS

Lenox D. Baker, M.D.
Duke University

Lenox D. Baker is Professor of Orthopedic Surgery and Director of the School of Physical Therapy at Duke University School of Medicine. He is also Medical Director of the North Carolina Cerebral Palsy Hospital, Executive Committee Chairman of Durham's Lincoln Hospital, and Consulting Orthopedist for the N. C. Division of Crippled Children and Department of Vocational Rehabilitation. Dr. Baker has received the Sertoma International Award for aid to crippled children and, from President Eisenhower, the Physician-of-the-Year President's Award for his contributions to employment of the physically handicapped.

CHILDREN'S BROKEN BONES

It has been 20 years since Blount and others began the crusade for conservative treatment of fractures in children, and still we occasionally see the tragic results of unnecessary surgery—surgery that may have been appropriate for similar fractures in adults, but is totally uncalled for in children. In general, the bones most frequently broken in children can be treated by simple manipulation and immobilization. Simple methods can give a perfect result in most every case because of the "molding factor", which works overtime in youngsters (Figure 1). Usually not only is surgery unnecessary; it may be hazardous. Nonunion, delayed union, and infection may be the result.

Fractures of the Forearm

Fractures of the forearm are excellent examples of the superiority of conservative treatment. In children under 12, they almost always are treated better by closed methods than by open. Fractures of the radial neck are good examples of this principle because their management differs so markedly from management of the same injury in adults. In the adult, manipulation and frequently surgery are needed to restore satisfactory function of a fracture with displacement and angulation. Even then, some residual disability is likely. In children, just the opposite is true. While alignment by manipulation is preferred, angulations of as much as 45° may be immobilized without alignment. The fracture will heal, and growth can restore the motility and contour of the radial head and neck. If the angulation is greater, open reduction may be indicated but never excision of the head of the radius.

Fracture of the proximal third of the ulna with dislocation of the radial head (Monteggia's fracture) is another example of the strikingly different management of children's fractures. Reduction of the dislocated radial head plus alignment of the ulna and immobilization by a well-applied cast are all that is needed. In contrast, the same injury in adults, most always requires internal fixation of the ulna.

Simultaneous fractures of both bones of the forearm are also handled differently in children than adults. Most often located in the *distal* third, they are frequently of the Greenstick variety. Although there is some disagreement on this point, I believe that angulations of the radius in the lower third of the forearm should be reduced; but end-to-end apposition is unnecessary. Likewise, to prevent deformity, Greenstick fractures should be aligned. To prevent restricted pronation and supination after healing, angulated fractures of the *middle* third of the forearm must be properly aligned.

Casts for fractures of the forearm should extend from the axilla to the knuckles posteriorly and to the midpalmar crease anteriorly. The elbow should be flexed at a 90° angle. When angulation is not completely reduced before casting, follow-up roentgenograms should be made frequently enough to be certain that angulation is not increasing within the cast. If it does, do not resort to wedging of the cast. In children, remanipulation and recasting with traction are better. After the formation of early callus, the main object, good alignment, can usually be achieved by manipulation. Slight overriding with side-to-side rather than end-to-end apposition is acceptable.

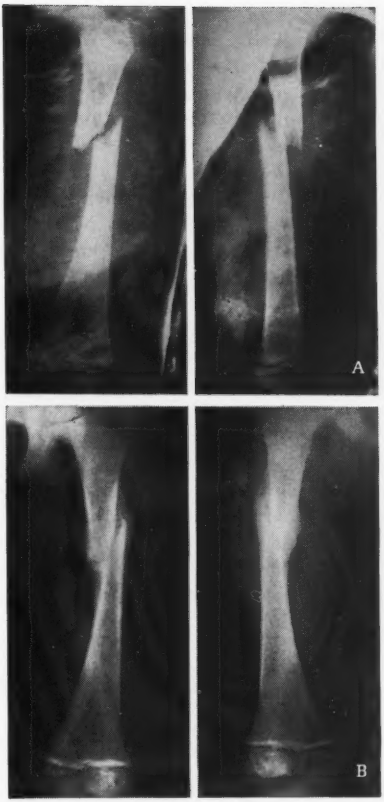


Figure 1 (A) This fracture of the femur of a three-year-old child illustrates the good results of conservative treatment. A note from the referring physician said, "I have attempted several methods of reduction and immobilization but failed to have proper alignments. It seems like this child will have to have open reduction." However, we judged the reduction adequate; hence the cast was not disturbed. Five weeks later, films (B) showed good callus, adequate length, and satisfactory alignment. Recovery was complete and uneventful.

Fractures of the Humerus

Fractures of the shaft are best treated by a hanging cast. Accurate reduction is unnecessary, as growth will compensate for minimal overriding. Likewise, considerable displacement of

fractures of the upper epiphysis is permissible; simple manipulation usually achieves adequate reduction. If not, surprisingly good results can be achieved by simple side-arm traction. Open reduction is never justified; when attempted, the usual result is poor alignment with consequent limitation of motion. Moreover, surgery runs the risk of producing aseptic necrosis of the epiphysis.

Considering the violence of the tumbles taken by active children, the frequency of supracondylar fractures is not surprising. Often they are caused by the impact produced when the child pitches forward on his outstretched hand. Supracondylar fractures, too, are reduced by traction. With good alignment and correct rotation, moderate posterior displacement of the distal fragment is permissible, but rotation must be corrected. Immobilization with the elbow at a 90° angle should give good results. In the presence of severe swelling or other signs of damage to soft tissue, manual reduction may be delayed. Suspension traction, or traction applied by a Dunlop sling for 48 to 72 hours, is then indicated. When the swelling subsides, the fracture can usually be reduced by gentle longitudinal traction under anesthesia. We make it a rule to hospitalize for at least overnight all patients with fractures in this area.

The dangerous complication of supracondylar fractures is vascular impairment or nerve injury. Prompt reduction, preferably by traction and elevation, is the best prophylaxis. If the radial pulse is detected before reduction, be certain that it is not interrupted during treatment. Prompt surgical intervention is justified in the presence of such warning signs as pain in the hand and swelling, cold, cyanosis, or pallor of the fingers.

Fractures of the Femur

For spiral fractures of the femoral shaft, so common in children, there are two, and only two, acceptable methods of treatment: traction and plaster fixation. Depending upon the age of the child, either Bryant's overhead traction or Russell's block and tackle traction will give excellent results. The use of Bryant's traction is limited to the very young and the unusually supple child. Even then every precaution must be taken to observe for circulatory embarrassment. Maintain traction until sufficient callus is formed to maintain reduction; then immobilize in plaster. End-to-end apposition of transverse fractures of the femoral shaft is undesirable; side-to-side apposition with ¼" to ½" overriding reduces the effect of overgrowth.

Fractures of the Tibia

Fractures of the tibia are also commonly of the spiral type. Cast fixation is usually sufficient. In the transverse fractures, however, manipulation is often required. A highly satisfactory method for reducing these fractures is to apply a plaster cast in two sections. One covers the thigh, the knee (bent at 90°), and the portion of the calf above the fracture. The other section covers the calf below the fracture, the ankle, and the foot. The back of the knee and ankle and the heel and Achilles tendon should be adequately but not overly padded. When the two sections of the cast have set, reduction under anesthetic by means of traction and, if necessary, manipulation is usually easy. The two sections of cast are then joined into one by application of additional plaster.

Even in children, surgery is sometimes necessary, particularly for fractures of the humeral epicondyles, neck or epiphysis of the femur, the patella, and the olecranon. Yet, as shown in the foregoing examples, most childhood fractures respond well to simple treatment.

QUESTIONS AND ANSWERS

Q. *How can rotation of the distal fragment in supracondylar fractures be controlled?*

A. This can be a difficult problem. Often rotation of the fragment can be controlled by casting with the forearm midway between supination and pronation, but a body cast with a shoulder spica may be needed.

Q. *Isn't surgery necessary to reduce separations of the distal radial epiphysis?*

A. This fracture in a child is comparable to Colles' fracture in adults; as in Colles' fracture, an anatomical reduction is desirable. However, minor displacement is preferable to the results to be expected from open reduction with its danger of injury to growing cells of the epiphysis.

Q. *How are fractures of the elbow with displacement reduced?*

A. If the displacement is great, good reduction of fractures of the trochlea, epicondyles, and, particularly, the capitellum can be achieved only by surgery. In contrast to fractures of the long bones, good reduction of fractures at the elbow is necessary to achieve good function and prevent ulnar nerve palsy. Fracture of the medial epicondyle is not so serious, but if displaced it too is best reduced surgically.

Q. *When should Bryant's traction be applied for fractures of the femur?*

A. Bryant's overhead traction is recommended for spiral fractures of the femur in supple children under 3. Until the age of 3, the hamstrings are still sufficiently long to permit flexing the hip at 90° with the knee straight. Bryant's traction not only can give excellent results, it is very convenient. Because it is portable, the child with close observation can be treated at home. It permits easy changing of diapers of an infant in traction.

Q. *What is the best method for reducing fractures of the epiphysis of the tibia?*

A. When a child injures his ankle, it usually takes the form of separation of the epiphysis. Never attempt to reduce the epiphyseal separation with a twisting or angulating motion. Instead, apply the reducing force *parallel* to the separation. For instance, if the epiphysis is displaced posteriorly, place the patient in a prone position with his toes over the end of the table and with two sandbags placed under the distal end of the

tibia. Then reduce the separation with a downward force on the heel. On the other hand, if the epiphysis is displaced anteriorly place the child in a supine position with sandbags under the distal tibia, and apply a downward force upon the foot. Similarly, lateral displacements should be reduced by applying parallel forces to push the epiphysis back into position.

Q. *What is the reaction of the child's parents when shown an x-ray of the femur without end-to-end apposition?*

A. Parents are sometimes understandably apprehensive when informed that anatomical reduction of their child's fracture is not to be attempted. I try to explain that if my child had a fractured femur, I would prefer reduction with side-to-side apposition and ½" to ¼" overriding, because healing is just as quick and overgrowth is less. Reassurance of a nervous mother is sometimes the most difficult part of treating fractures in children. Let me paraphrase Congressman John Allen who, 100 years ago, said of the Mississippi Delta, "Braver men never rode finer horses across more fertile fields to see more beautiful women than those who live in the Mississippi Valley." I say, "More precious patients never brought more important injuries across a doctor's threshold for simpler therapy than those children who have suffered a fracture of an extremity."

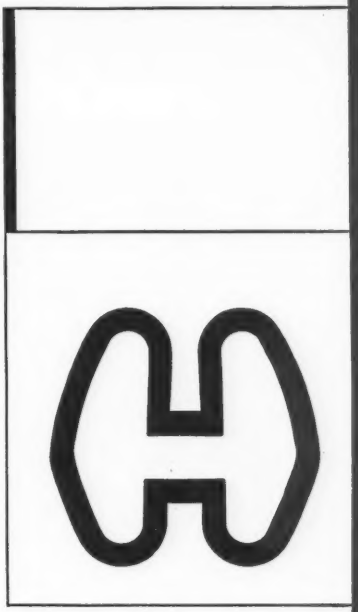
When starting thyroid replacement therapy in hypometabolism or hypothyroidism . . .

CYTOMEL®

brand of liothyronine

This pure synthetic compound offers these 5 significant advantages:

1. Rapid clinical improvement
2. Easy, sensitive dosage adjustment
3. No tolerance or cumulative effect
4. Value as a diagnostic aid
5. Effectiveness in many thyroid-resistant patients



PRESCRIBING INFORMATION

ADMINISTRATION AND DOSAGE: Dosage should be adjusted according to the severity of the condition and the response of the patient.

Most patients should be started on 25 mcg. of 'Cytomel' daily. To increase dosage to recommended maintenance levels for these patients, increments of 12.5 or 25 mcg. may be made in the daily dosage at intervals of one or two weeks. Dosages in the range of 100 mcg. daily, and higher, are well tolerated by many patients.

When starting dosage is 5 mcg. daily (as in myxedema, male infertility, simple goiter and in patients being switched from thyroid, L-thyroxine, or thyroglobulin), increments of 5 or 10 mcg. may be made in the daily dosage at intervals of one or two weeks. When dosage reaches 25 mcg. daily, increase as described above.

'Cytomel' is usually administered in divided doses.

Note: In geriatric patients or in children always start with 5 mcg. daily and adjust dosage in increments no greater than 5 mcg.

Indication	Recommended Starting Dose	Recommended Maintenance Dose
Hypometabolism Mild Hypothyroidism	25 mcg. daily	25-75 mcg. daily (Smaller doses may be fully effective in some patients.)
Myxedema	5 mcg. daily	50-100 mcg. daily
Female Reproductive Disorders	25 mcg. daily	25-50 mcg. daily
Male Infertility (Based on sperm count or sperm motility responses after two to four weeks of treatment at a given dosage level, the daily dosage may be increased by 5 or 10 mcg. If after further treatment the desired response has still not been obtained, the daily dosage may again be increased. Although total daily dosage usually need not exceed 25 mcg., as much as 50 mcg. daily may be used if necessary.)	5 mcg. daily	10-25 mcg. daily
Simple (non-toxic) Goiter	5 mcg. daily	25-75 mcg. daily

SPECIAL CONSIDERATIONS AND CAUTIONS: Tachycardia, excitability, headache, or excessive sweating are signs of overdosage. Medication should be interrupted until the unpleasant symptoms disappear, and then resumed in smaller doses. Since the return to pretreatment status is rapid, 'Cytomel' can usually be resumed at the desired dosage after one to two days.

When a subnormal BMR exists as part of the clinical syndrome of hypometabolism or hypothyroidism, administration in excessive dosage will cause elevation of BMR to levels above normal.

'Cytomel', unlike various forms and fractions of thyroid, will not cause elevation of the blood protein iodine level.

Endogenous thyroid gland function, reflected particularly by I^{131} uptake, may be depressed by 'Cytomel' administration. Depression of this function is most apt to occur with higher dosages (greater than 75 mcg. daily). Experience to date indicates that this effect is not clinically harmful. There have been no unfavorable sequelae in reported instances where 'Cytomel' therapy has been discontinued after depression of I^{131} uptake occurred. In such cases this function has promptly returned to normal after discontinuance of 'Cytomel'.

Since 'Cytomel' is physiologically related to thyroxine, it is not recommended for use in the presence of angina pectoris, in other cardiovascular disorders, or ischemic states. However, if it is used in the presence of such conditions, the starting dosage should never be more than 5 mcg. daily. If dosage is increased, it should be in increments of no more than 5 mcg. daily at approximately two-week intervals.

Hypopituitarism, morphologic hypogonadism and nephrosis should be ruled out before 'Cytomel' is administered.

CONTRAINDICATION: Addison's disease.

FORMULA: Each 'Cytomel' tablet contains 5 mcg. or 25 mcg. of liothyronine (L-triiodothyronine or LT3), as the sodium salt; 25 mcg. of 'Cytomel' is calorigenically equivalent to approximately 1 gr. of thyroid.

AVAILABLE IN TWO DOSAGE STRENGTHS: 25 mcg. (scored) tablets in bottles of 100 and 1000; 5 mcg. tablets in bottles of 100.

Prescribing information adopted Jan. 1961

SK&F Smith Kline & French Laboratories

PSYCHIATRY

Charles W. Wahl, M.D.
University of California Medical Center

Charles W. Wahl is Assistant Professor and Chief of the Division of Psychosomatic Medicine, Department of Psychiatry, University of California Medical Center. He serves as consultant in psychiatry for the Sepulveda V.A. and Camarillo State Hospitals. He received his M.D. from the University of Kansas, and his residency training at Elgin State Hospital, Cushing V.A. Hospital, Massachusetts General Hospital, and at The Maudsley Hospital, University of London. Dr. Wahl has published articles in various professional journals, and has contributed chapters to three books.

THE DYING PATIENT

We physicians are taught in great detail about life – its nature, its attributes, the diseases that threaten it, and how to preserve and extend it. Indeed, our training is so exhaustive that we become thoroughly familiar with the etiology, signs, symptoms, diagnosis, treatment and prognosis of diseases we may never encounter even once during a lifetime of busy practice. Yet, and I have always thought it rather remarkable, almost nowhere during our formal education do we receive guidance concerning the one problem we know we will face sooner or later – the patient who is dying. Why this particular medical responsibility (I think all physicians will agree they bear at least some responsibility to help the patient meet this problem) should receive so little academic attention need not be discussed here, but a few practical comments may be in order.

The goal of the management of a terminally ill patient is to enable the patient to die, if he must die, with as much dignity, serenity, and possession of his human faculties as possible. The following suggestions may help you achieve this goal.

The Patient's Hope

As far as his reaction to death is concerned, modern man has not advanced very far beyond his primitive ancestors. Like them, terminally ill patients, with few exceptions, are able to ignore or discount seemingly obvious and overwhelming evidence that their death is imminent, no matter how slight the rational probability of survival. They flee from the reality of death with purpose and persistence, and employ defenses so patently magical and regressive that they would be ludicrous – even to the patients

themselves – if they were used to the same degree under any other circumstances. Even patients who say they recognize and accept the fact, patients who have been told "the truth" flatly by their physicians, continue to hope and find comfort in such hope. In general, anything that will strengthen such defenses and encourage such hope will be helpful; anything that would weaken or discourage them would not.

Telling the Patient the Truth

In my opinion, it is usually better not to tell the patient his true prognosis if it is a fatal one. Whether you can agree with this opinion or not, it is always wise to learn something about the dying patient's ability to deal with emotionally painful and disturbing situations in the past when trying to decide whether to tell him he is dying. No dying patient can adjust to this situation any better than he has to stress situations in the past, and the average patient, in the face of this very special and unique threat, will probably be less able to adjust than he ordinarily would be. Paradoxically, it is usually the patient who is most insistent that he be told the truth who is least equipped to handle it.

What Should You Tell Him?

The patient may be dying, but he is not likely to be a fool. Despite his eagerness to continue hoping, he will probably realize that his condition is serious and will not accept or believe hearty reassurances like "Nothing to worry about – we'll have you up and around in no time." Such transparently false cheerfulness will not help the patient, and the suspicion you create may make suspect any other advice you offer. A statement like "You have a serious problem, but no illness is without hope and you should remember that" is much more likely to be believed and reassuring.

Do Not Isolate the Patient

The Greeks said that the most horrible of ills is not to die, but to die alone. I think they were right and that the dying patient should not be isolated from friends and relatives or the hospital staff any more than necessary. Regular and predictable contact with the physician implies continuity–continuity of care to the patient's conscious mind; continuity of life to his unconscious. It implies a promise, "I will see you again tomorrow at the same time, and you have nothing to fear in the interim." And this dependable certainty alone helps make the patient more comfortable. For just this reason, of course, you must be very careful not to omit a promised visitation. It is much better to set a schedule of visits you can reasonably expect to meet, than to be unrealistically optimistic and then have to cancel or miss appointments. Incidentally, though relatives should be encouraged not to isolate the patients, you should not permit constant or unduly prolonged visits that the patient may interpret as a "death watch."

"Trading Up" Illnesses

You should help the patient transfer his attention and concern from his incurable illness, and focus them on other, curable ones he may have, or on symptoms you can relieve. You should even encourage hypochondriasis and listen with interest and attention to all his complaints, particularly ones related to intercurrent infections, colds, skin rashes, etc., that can be

eliminated. These complaints should be treated vigorously. By "trading up" such objectively minor illnesses to a more serious subjective level, the patient can receive enormous reassurance and relief as your attempts to control them are successful.

To the same end, you should deliberately focus attention on the patient's "immortal physiology," such as the processes of digestion and elimination. The exaggerated concern of aged patients with these processes is common, and it is remarkable how often the terminally ill patient regresses to such infantile logic and conception of disease—"If I just avoid drafts and have a good bowel movement, I can never be ill." It is not wise, however, to utterly ablate all pain. To feel nothing is to be dead, and the terror that may be produced by complete analgesia can far outweigh its advantages. Since ataraxic or sedative drugs may produce a similarly terrifying sense of isolation and detachment from reality, they should be used, if at all, with discretion.

The Patient's Demands

When listening to the patient's complaints, you should identify the key words he uses, and pay particular attention to those that express fear of death. The terminally ill patient may have a recurrence of fear of the dark, or of closed doors, of lying recumbent, of numbness or coldness, and the words he uses to express these fears often reveal the primary anxiety—"I'm deathly afraid of the dark," "I feel boxed in when the door is closed." To reduce such anxiety and fear of death, all such demands, and many are quite idiosyncratic, should be met as unobtrusively as possible.

Touch the Patient

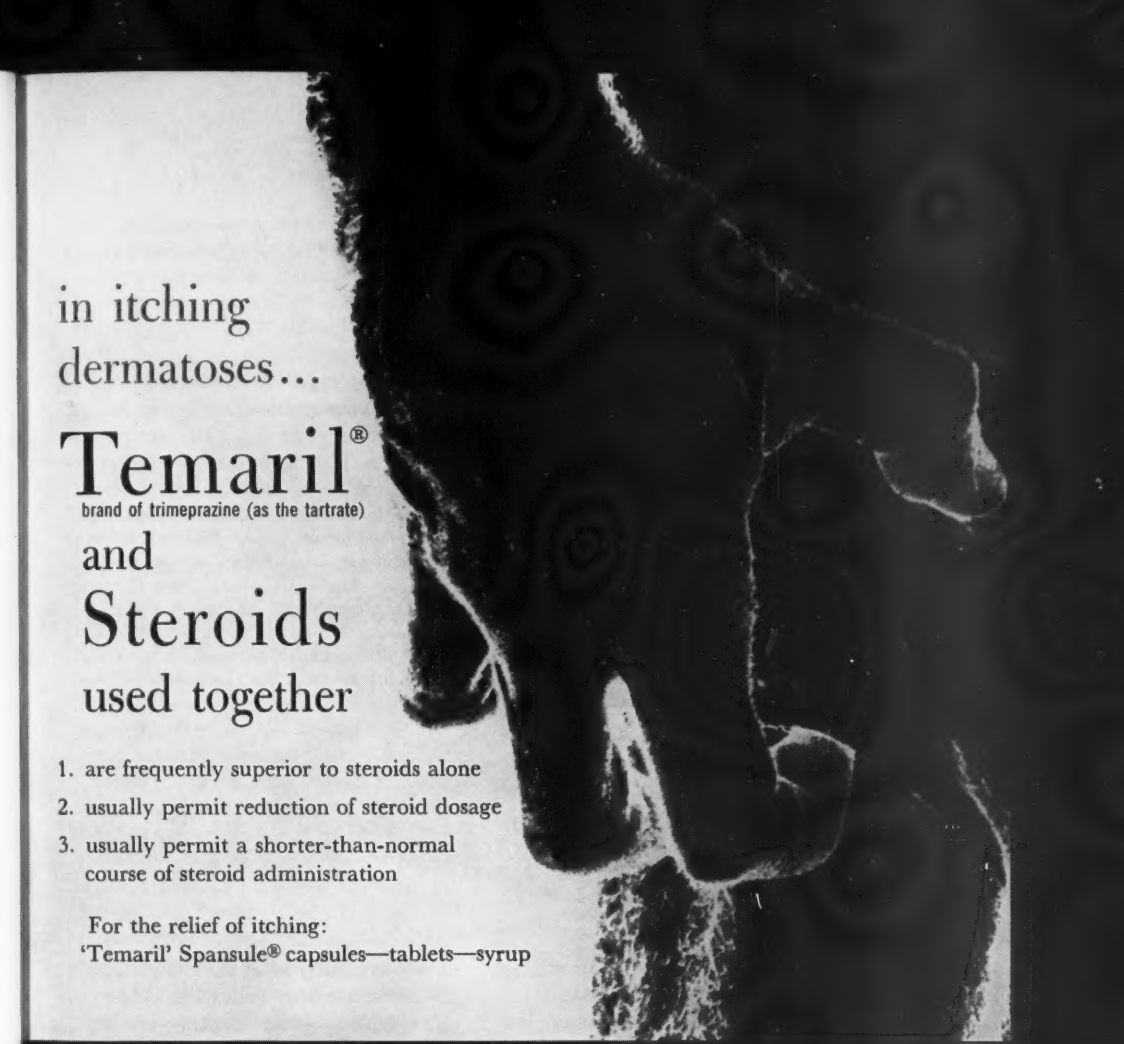
The touch or caress is the most primitive and basic nonverbal comforting technique we possess. It can communicate a solace or comfort to the disturbed or frightened patient that words can never produce. In addition, it assuages the unconscious fear of being "untouchable," – the dying or feared thing. Frequent backrubs or massages, for example, engender both physical and psychic well-being.

Encourage Planning for Future

The patient should never be treated as if he had no future. All patients should be encouraged to plan for themselves and their family, particularly for their children. Children are, in the unconscious, "the fruit of our loins," extensions of ourselves, living defenses against the fear of being blotted out, and terminally ill patients can derive comfort and satisfaction from their visits and from helping them plan their future. In addition, such family contact is also a service to the patient's survivors, whose guilt and sadness are relieved by these opportunities to help their loved one.

Simple Measures Usually Enough

These simple measures, employed by a warm and empathetic physician, and acting in concert with the powerful defenses the seriously ill person can call upon, usually enable the terminally ill patient to cope with his situation successfully. In a small minority however, these measures fail, and the prospect of imminent death may provoke a terror, depression, or apathy that can lead to psychosis. The treatment of choice for these patients is intensive psychotherapy, and consultation should be arranged as soon as possible.



in itching dermatoses...

Temaril®

brand of trimeprazine (as the tartrate)

and Steroids used together

1. are frequently superior to steroids alone
2. usually permit reduction of steroid dosage
3. usually permit a shorter-than-normal course of steroid administration

For the relief of itching:
'Temaril' Spansule® capsules—tablets—syrup

'Temaril' is an oral medication specifically for the relief of itching. It has been found effective in relieving pruritus accompanying dermatoses of allergic, inflammatory, metabolic, hemovascular and psychic origins, as well as those whose etiology is not clearly understood.

INDICATION: 'Temaril' is indicated for the treatment of mild and severe pruritus, whether acute or chronic.

DOSAGE AND ADMINISTRATION: Dosage with 'Temaril' should always be adjusted according to the severity of the symptom and the response of the patient.

	Usual Dosage	Resistant Cases
Adults	tabs.: 1 (2.5 mg.) q.i.d. caps.: 1 (5 mg.) q12h	tabs.: 2-4 q.i.d. caps.: 2-3 q12h
Children (ages 7-12)	tabs.: 1 t.i.d. caps.: 1 at night	tabs.: 2 t.i.d. caps.: 1 q12h
Children (ages 3-6)	tabs.: 1 t.i.d. syr.: 1 tsp. (2.5 mg.) t.i.d.	tabs.: 1 q.i.d. syr.: 1 tsp. q.i.d.
Children (ages 2 and under)	syr.: ½ tsp. t.i.d.	syr.: ½ tsp. q.i.d.

NOTE: Total daily dosage should not exceed 5 mg. for children ages 2 and under, 10 mg. for children ages 3-6, or 15 mg. for children ages 7-12. The physician should caution parents not to administer more than prescribed dosage to children.

When itching is a nighttime problem, larger doses (in adults: 5 or 10 mg.) should be administered at bedtime, with daytime dosage adjusted accordingly.

SIDE EFFECTS: Mild and temporary drowsiness may be encountered. Dizziness, dryness of the mucous membranes and gastrointestinal upsets have occurred occasionally. All of these effects usually disappear after a few days of medication. Persistent drowsiness may be overcome by reduction of dosage.

CAUTIONS: Clinical experience has demonstrated that 'Temaril', a phenothiazine derivative, has a wide margin of safety and that there is little likelihood of blood or liver toxicity, or neuromuscular reactions (extrapyramidal symptoms). The physician should be aware, however, of their possible occurrence, and patients should be kept under regular observation.

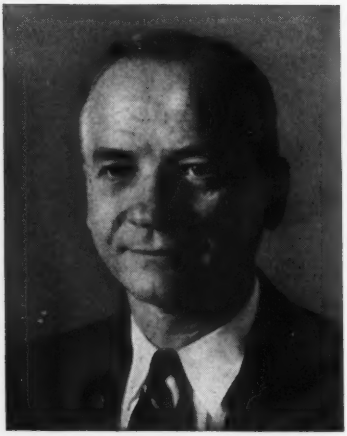
FORMULA: Each tablet and each 5 cc. teaspoonful of 'Temaril' Syrup contains trimeprazine, 2.5 mg., as the tartrate. (The syrup contains alcohol, 5.7%.) Each Spansule® sustained release capsule contains trimeprazine, 5 mg., as the tartrate.

SUPPLIED: Tablets, in bottles of 50 and 500; syrup, in 4 fl. oz. bottles; Spansule® capsules, 5 mg., in bottles of 30.

SK&F Smith Kline & French Laboratories

Prescribing information adopted Jan. 1961

GASTROENTEROLOGY



Thomas E. Machella
University of Pennsylvania

Thomas E. Machella is Associate Professor of Medicine at the University of Pennsylvania School of Medicine and is Chief of the Gastroenterology Section of the Medical Clinic (Kinsey-Thomas Foundation). A member of the American Society for Clinical Investigation and the American Federation for Clinical Research, Dr. Machella is widely known for his research on the causes of the dumping syndrome.

MECHANISM AND TREATMENT OF THE POSTGASTRECTOMY DUMPING SYNDROME

When the size of the stomach is decreased as it is after a subtotal gastric resection, food may enter the small intestine too soon after it is eaten. As a result, a variety of untoward reactions may occur, one of which is known as the dumping syndrome. Actually, there are two varieties of the dumping syndrome, the early postprandial and the late postprandial, but it is the early one that is seen more frequently and is the more difficult to manage.

The Early Dumping Syndrome

The syndrome is not, of course, an invariable consequence of gastrectomy and may not occur in every patient. But when it does, it usually develops shortly after the patient eats the first meal or so following surgery. Its symptoms may consist of any one, several, or all of the following: weakness, sweating, palpitation, vertigo, abdominal cramps, and collapse. The discomfort the symptoms cause may be mild on one occasion yet so severe on another that the patient is obliged to lie down until they subside. In some people the syndrome will occur after every meal, in others only after certain foods are eaten. The persistence of the condition also varies, lasting for only a month or two in some, or for years in others.

Mechanism

In the digestive process, the normal

stomach acts as a reservoir for the gastrointestinal tract and as such can expand without increasing intragastric pressure. But after gastrectomy, there may be so little stomach left that it cannot fulfill this function properly. Instead of digesting and diluting its contents, then slowly releasing them over a 2½- to 3-hour period, it releases them promptly into the small intestine. The small intestine, however, is not as large as the stomach and is not as adjustable. So a sudden increase in the volume of its contents increases the intraluminal pressure, distending the intestine and producing the symptoms of the dumping syndrome.

This increase in the volume of the small intestine can, of course, depend on how much a person eats at any one time, but in the dumping syndrome it is *what* a person eats that counts. The reason for this is that different foods have different osmotic properties. Sugars, for instance, are high in osmotic activity. The ingestion of a solution that has a high concentration of sugar usually makes the stomach contents hypertonic, setting off the osmotic process that, by rapidly drawing fluid from the blood stream, dilutes the sugar solution until it becomes isotonic. Protein hydrolysates and solutions of electrolytes will have the same effect of increasing volume. On the other hand, a mixture of starch and water of the same volume and concentration as the sugar solution will not bring about the symptoms because its osmotic activity is very low.

The resected stomach dumps its contents, still hypertonic, into the small intestine where fluid enters from the blood stream. The intraluminal pressure and motility both increase, thus inducing the dumping syndrome or abdominal cramps and diarrhea.

Other objective manifestations that have been shown to occur during the dumping reaction include glycosuria, elevation in blood pressure, tachycardia, electrocardiographic changes, decrease in plasma potassium and phosphate, decrease in circulating eosinophils, urinary retention of sodium and chloride, increase in urinary excretion of uric acid, and transient decrease in plasma volume.

Some of the systemic manifestations that accompany the reaction are similar to those that follow the administration of cholinergic and adrenergic drugs, and suggest the possibility that there is a reflex stimulation of both the sympathetic and parasympathetic divisions of the autonomic nervous system. Other systemic changes may also occur; these vary, of course, depending on the chemical nature of what the person eats.

Treatment

Certain drugs and compounds administered before meals have been reported to prevent the dumping syndrome. These include atropine, ephedrine, phenyl-ethyl-methyl-hydantoin, potassium chloride, sodium bicarbonate, and tetraethylammonium. But in my experience, none of them do much good. I found they either did not work, or when they did appear to be of benefit, they caused such troublesome side effects that their routine use was impractical. I have had better results by having the patient eat foods such as fats, starches, and crude protein that have no or relatively little osmotic activity. Having the patient take fluids

between meals instead of during meals is also helpful. As in many other conditions, however, an ounce of prevention is worth a pound of cure, and in this case the ounce of prevention lies in preserving the reservoir function of the stomach when a subtotal gastric resection is performed.

Late Dumping Syndrome

The late postprandial dumping syndrome is due to hypoglycemia. The symptoms occur 1½ to 2½ hours after a meal instead of during or shortly after the meal. They are caused by an increased secretion of insulin induced by the hyperglycemia that occurs in response to the meal. It is most likely to occur during periods of increased mental tension and can be prevented by a diet high in fat and crude protein but low in carbohydrate.

QUESTIONS AND ANSWERS

Q. *Are there any other theories to account for the dumping syndrome?*

A. Yes. Hypoglycemia, hyperglycemia ("hyperglycemic shock"), irritation of the jejunum, and allergy to milk (the porridge syndrome) are among those that have been suggested. However, distention of the small intestine is the most commonly accepted.

Q. *What role do blood sugar levels play in producing symptoms of the early postprandial dumping syndrome?*

A. None. In someone who has the dumping syndrome this can be demonstrated by comparing the effects of orally administered glucose in a hypertonic solution with those caused by an equivalent amount of intravenous glucose. Blood sugar levels in both instances will be the same. But only the orally administered glucose will induce the symptoms.

Q. *Would it be possible to get a list of the foods that should be avoided because their osmotic activity is high?*

A. Write to me, in care of CONSULTANT, and I will see that you get one.

Next month in CONSULTANT:

Office Management of Stasis Ulcers—Reginald Farrar, M.D. describes an effective treatment for chronic stasis ulcers—"an old method, and an easy one to use, but for some reason is not used as often as it should be."

Treatment of the Adolescent—J. Roswell Gallagher, M.D., gives some useful advice on how to help your adolescent patients during their period of rapid physical, emotional and psychological change.

BREAKS THE HABIT OF COMPULSIVE OVEREATING

'Eskatrol' *Spansule* capsules provide daylong control of appetite *and* relief of the psychic stress that causes overeating. Because the tranquilizer component of 'Eskatrol' controls emotional stress, your patient has a better chance of staying on his diet —even for prolonged periods of time.

ESKATROL® SPANSULE®

brand of sustained release capsules

Prescribing Information

FORMULA: Each 'Eskatrol' *Spansule* sustained release capsule contains Dexedrine® (brand of dextro amphetamine sulfate), 15 mg., and Compazine® (brand of prochlorperazine), 7.5 mg., as the dimaleate, distributed among hundreds of minute pellets with varying disintegration times. A therapeutic dose is released immediately and the remaining medication, released slowly and without interruption, sustains the effect for 10 to 12 hours.

IN OVERWEIGHT PATIENTS: 'Eskatrol' *Spansule* capsules are indicated in overweight patients, particularly in those who depend on eating for psychologic release.

'Eskatrol' *Spansule* capsules provide not only daylong control of appetite but also relief from the emotional stress associated with overeating and with dieting. The desire to eat is reduced and patients, particularly the so-called "compulsive eaters," feel better and are able to adjust to the weight-reducing program—*even for prolonged periods of time.*

RECOMMENDED DOSAGE: One 'Eskatrol' *Spansule* capsule daily, taken in the morning.

SIDE EFFECTS: Side effects (chiefly nervousness and insomnia) are infrequent, and usually mild and transitory.

CAUTIONS: Clinical experience has demonstrated that 'Eskatrol' (containing the phenothiazine derivative, 'Compazine') has a wide margin of safety and that there is little likelihood of blood or liver toxicity or neuromuscular reactions (extrapyramidal symptoms). The physician should be aware, however, of their possible occurrence.

'Eskatrol' *Spansule* capsules should be used with caution in the presence of severe hypertension, advanced cardiovascular disease, or extreme excitability.

Adopted Jan. 1961

AVAILABLE: In bottles of 30 and 250 capsules.

Smith Kline & French Laboratories

SK&F

DERMATOLOGY

E. William Rosenberg
University of Miami Medical School

E. William Rosenberg is an Assistant Professor of Dermatology at the University of Miami Medical School. He received his medical education at the University of Pennsylvania and took his residency at Massachusetts General Hospital. Dr. Rosenberg has been writing since his medical school days when he worked part time for the International News Service. He recently co-authored a chapter in a dermatology textbook and also wrote a section for CURRENT THERAPY, 1961 about the treatment of herpes simplex. His interest in oral aphthae is a natural consequence of the research he has done on herpes simplex.

THE PROBLEM OF CANKER SORES

Some diseases seem to elude medical attention not because of their great rarity, but, instead, because of their great commonness. Such diseases are readily diagnosed by the patient's relatives, friends, and neighbors who usually volunteer that they get the same thing themselves, and, furthermore, that there is nothing much good for it.

This appears to be the case with recurring oral aphthae (a term that goes back to Hippocrates) which are more commonly called canker sores. A recent British survey indicated that 1 in 5 persons in the general population suffer from them at one time or other in their lives. For most, the sores come infrequently and present only a minor inconvenience, but for others the disease can be severe, unrelenting, and almost totally disabling.

What Causes Them?

The cause of recurring oral aphthae is unknown. One thing seems certain (despite some medical articles and considerable lay prejudice) aphthae are *not* due to the herpes simplex virus. Recurring herpetic fever blisters occur around the mouth, not inside it. Many patients who suffer from episodic aphthae relate the disease to emotional factors. In women, for example, this disease, like most obscure diseases, is often blamed on either the menstrual flow or its cessation at the menopause. Food allergy to chocolate, walnuts, etc., is another commonly blamed offender although it is certainly not responsible for the vast majority of cases.

Incidence

The condition is common and somewhat more prevalent in women. It

often begins in adolescence or early adult life but may occur at any age from childhood on.

Diagnosis

The lesions of recurring aphthous stomatitis occur on the inner aspects of the lips, the buccal mucosa, the tongue, and the gums. They can occur anywhere inside the mouth but are less common on the tonsillar pillars, helping to differentiate them from the lesions of herpangina.

Often the patient will sense an outbreak before it appears, complaining of a peculiar burning or stinging sensation somewhere in the mouth. The lesion begins with a small area of redness. Soon thereafter, the site develops into a superficial slough, about 1 to 3 mm. in size, covered by a white-gray membrane. The extreme amount of pain reported often seems inconsistent with the small size of the lesion. Later, the lesion may enlarge to nearly 1 cm. in diameter and become much deeper. Outbreaks consist of anything from a single small lesion to involvement of almost the entire oral mucosa.

A history of previous attacks and the absence of gross cervical lymphadenopathy help to differentiate aphthosis from the unusual occurrence of primary herpetic stomatitis in an adult. Other conditions with which aphthae may be confused include erosions from ill-fitting dentures, drug eruptions, erythema multiforme, pemphigus, and herpangina. Oral manifestations of cyclic neutropenia and the leukemias can be differentiated by blood studies. The nosologic status of conditions like Behçet's syndrome in which aphthous ulcerations are associated with eye and genital involvement is unclear; they may be closely related. In most cases, however, the diagnosis is straightforward and easy.

Course

There is a wide variation in the amount of trouble caused by aphthae. For most patients the tendency to recurring oral ulcerations is extremely chronic, lasting from 10 to 20 years or more. The majority of patients suffer from only a few small ulcers that occur less than 3 or 4 times a year and heal spontaneously in 1 to 3 weeks. Other patients who suffer similarly infrequent but more severe attacks are subject to a periodic breakdown of large areas of oral and lingual mucosa associated with great pain, inability to eat, and a foul breath. It may well be that much of what is called "trenchmouth" is this sort of severe apthhous outbreak, secondarily overrun by the oral flora. Finally there is a small number of unfortunate persons who suffer almost continually from aphthae of greater or less severity. They get a new outbreak every 2 or 3 weeks and the lesions no sooner heal than others appear. When they get the severe ulcerative form of the disease, their misery is extreme and nearly constant and may last over many years.

Treatment

The list of suggested treatments runs from aureomycin to lactobacillus to trichloroacetic acid to x-ray and is nearly endless. Since aphthae are common, occur at irregular intervals, and are always self-healing, they afford a perfect opportunity for the physician to choose some favorite treatment that he is convinced is effective

(but isn't). However, there is some value in those treatments the doctor himself believes in because there is some evidence that the interested, optimistic physician helps, perhaps by suggestion, to shorten and ease attacks.

Repeated smallpox inoculations as a means of preventing attacks is an excellent example of the role that suggestion plays. This treatment is frequently used in the therapy of recurring herpes simplex and came into favor when aphthae were thought to be a manifestation of herpes infection. Since we now know that this is not true, we must assume that any beneficial effects are due to suggestion — which is probably the case in herpes, too.

Steroid Therapy

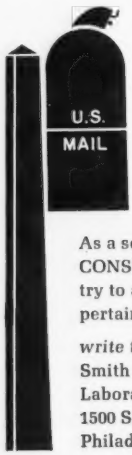
Some studies, and my own experience, indicate that the corticosteroids given in adequate doses are highly effective in shortening and aborting an attack. Usually 4 tablets of one of the standard preparations (like prednisone or prednisolone) taken for 3 to 6 days will bring satisfactory improvement.

Some patients seem to get by with a lower total dose of steroid if they use one of the topically-active forms of corticosteroid (hydrocortisone is, cortisone is not; prednisolone is, prednisone is not) and suck on the tablet until it dissolves instead of swallowing it. The recently introduced "Kenalog in Orabase" (Squibb) includes the topically-effective triamcinolone acetonide in a special ointment base that will stick to the oral mucosa. It has seemed to be of some limited benefit in a few cases.

The steroids are of most value in patients who get infrequent but severe attacks. They are probably not justified in the sporadic mild attack. In patients with continuing severe attacks, the considerations of extensive, long-term use of steroids are the same as in arthritis and other disorders where their usefulness in alleviating symptoms must be weighed against possible side effects.

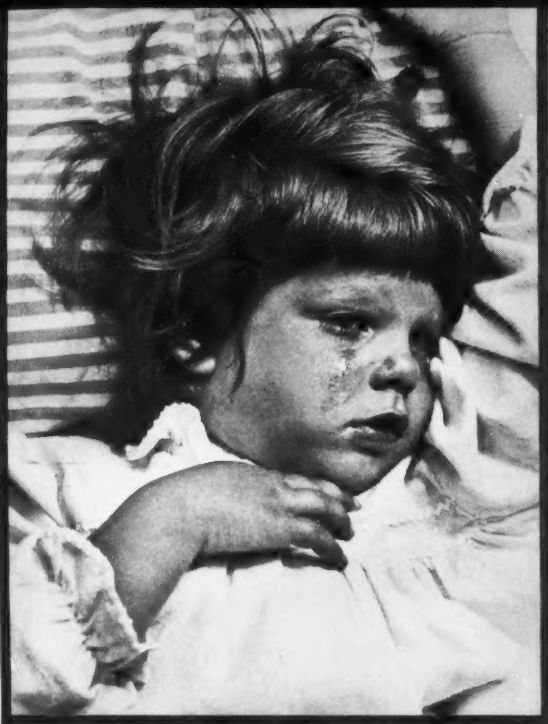
Patients with extensive erosions may obtain some symptomatic relief with "Xylocaine Viscous Syrup," especially before attempting to eat. Cold malted milkshakes are useful in supporting patients in too much pain to eat.

CORRESPONDENCE



As a service to readers, CONSULTANT's authors will try to answer any question pertaining to their topics.

write to: CONSULTANT
Smith Kline & French Laboratories
1500 Spring Garden Street
Philadelphia 1, Pennsylvania



TO RELIEVE SYMPTOMS OF

THE COLD COMPLEX IN CHILDREN—

Coplexen® *Liquid*

A SINGLE PREPARATION,

SPECIALLY DESIGNED FOR CHILDREN—

NOT ONLY RELIEVES COUGH

NASAL CONGESTION

FEVER

MUSCULAR ACHES AND PAINS

BUT ALSO CONTROLS

IRRITABILITY

RESTLESSNESS AND INSOMNIA

Prescribing Information

INDICATIONS: 'Coplexen' is indicated for use in children to control cough, nasal congestion, fever, muscular aches and pains, irritability, restlessness and insomnia. Recommended for the cold complex in children, as seen in coryza, rhinitis, pharyngitis, tonsillitis, laryngitis, sinusitis, bronchitis, pneumonitis and other acute upper respiratory infections.

In croup: While experience is still limited, 'Coplexen' Liquid has demonstrated unusual effectiveness in relieving this distressing syndrome.

USUAL DOSAGE:

Weight	Dosage
10 to 24 lbs.	½ tsp. at 4- to 6-hour intervals, if needed
25 to 74 lbs.	1 tsp. at 4- to 6-hour intervals, if needed
75 lbs. or more	1 or 2 tsp. at 4- to 6-hour intervals, if needed

The bedtime dose may be repeated, if needed, to induce sleep.

Total 24-hour dosage for children 10-24 lbs. should not exceed 3 tsp.; for children 25-74 lbs., 6 tsp.; for children 75 lbs. and over, 9 tsp.

'Coplexen' Liquid may be administered concomitantly with antibiotics, sulfas, or aspirin. If administered with central nervous system depressants, dosage should be adjusted carefully to avoid possible excessive sedation.

CAUTIONS: Side effects, mainly unwanted sedation, are rarely seen with 'Coplexen'. Since it contains a phenothiazine derivative (trimeprazine), patients taking 'Coplexen' should be watched for possible occurrence of agranulocytosis or other serious side effects. Paradoxical stimulation with muscle incoordination has been rarely reported with trimeprazine. Should it appear, 'Coplexen' administration should be halted; no other measures are needed.

FORMULA: Each 5 cc. teaspoonful contains trimeprazine as the tartrate (Temaril®), 2 mg.; phenylpropanolamine hydrochloride, 10 mg.; acetaminophen, 120 mg.; alcohol, 10%.

AVAILABLE: In a soothing fruit-flavored liquid in 12 fl. oz. bottles; usual prescription size, 3 fl. oz.

Prescribing information adopted Jan., 1961

SK&F

SMITH KLINE & FRENCH LABORATORIES

ENDOCRINOLOGY

Alfred M. Bongiovanni, M.D.
University of Pennsylvania

Alfred M. Bongiovanni is Associate Professor of Pediatrics at the School of Medicine of the University of Pennsylvania and Director of the Endocrine Division of Children's Hospital in Philadelphia. The author of 90 articles on pediatric endocrinology, he is a recipient of the Kolmer Medal and the Ciba Award of the Endocrine Society. He is a member of the American Academy of Pediatrics, the Pediatric Research Society, the American Society of Clinical Investigation, and the Pediatric Panel of the United States Pharmacopeia.

HORMONES AND FETAL HAZARDS

The management of pregnancy in women with chronic disorders, or who develop acute disorders, is a challenging problem. In these women, the application of drugs – however safe they may be otherwise – is complicated by the need to consider the possibility of a harmful effect on the fetus. We all know, for example, that large doses of vitamin K and certain long-acting sulfas are likely to produce hyperbilirubinemia in the infant. We could cite many similar examples. However, in this paper, I would like to focus attention on the fetal hazards related to the commonly used hormones and their related compounds.

Goitrogenic Drugs

At the Children's Hospital in Philadelphia, we have seen six infants born with large goiters that were accompanied by dyspnea and other alarming symptoms associated with compression of neck structures. In five of these cases, the mothers had received iodides or thiourea compounds during pregnancy for alleviation of thyrotoxicosis or allergies; and, the dosage of antithyroid drugs was fairly high, actually more than was strictly necessary. It is supposed that goitrogenic drugs produce enlargement of the fetal thyroid gland by interfering with the synthesis of thyroxine which, in turn, causes a rise in endogenous fetal thyrotropin. So, whenever goitrogenic drugs are truly necessary in a pregnant woman, it is important to use the minimal effective dose, and to give concomitantly thyroid during the last weeks of gestation to suppress thyrotropin. Fortunately, thyroid hormone—though it is used frequently during pregnancy – has not been known to produce any damage to the infant.

Androgens

There is much evidence to prove that androgenic hormones will affect the

external genitals of the female (but not the male) fetus if ample doses are administered during certain critical periods of gestation. Such virilizing effects have occurred even with the newer androgens reputed to have only anabolic action; there are definite reports of pseudohermaphrodism in female infants whose mothers received androgenic steroids during pregnancy. Inasmuch as there is no sound rationale for the use, during pregnancy, of primary androgens such as methyltestosterone or closely related derivatives, they should be abandoned at once.

Estrogens

Various estrogens are widely prescribed for the treatment of habitual or threatened abortion, but fortunately seem to affect the fetus only rarely. Only one example of possible feminization of the male fetus has been reported. Strangely enough, however, there have been more frequent instances of paradoxical masculinization of the female; I have personally seen masculinization in 4 female infants all of whose mothers received large doses of estrogen during pregnancy. Although masculinization by estrogens seems irrational, it is an effect which has been observed repeatedly by experimental embryologists and may be attributable to indirect action via the adrenal gland.

Progestins

Many of the progestational steroids, supposedly of value in threatened abortion, clearly have androgenic action and have been implicated in cases of female pseudohermaphrodism. Some progestins are known to be more virilizing than others; in our experience, two (Provera® and Delalutin®) have been relatively free of virilizing effects. The over-all incidence of masculinization related to the administration of progestins is low. Nevertheless, in light of the gravity of the fetal malformation involved, it is important to consider the actual value of these hormones in treating threatened or habitual abortion. The question is not yet settled but much of the evidence suggests that the progestins are currently overused. First of all, there is no absolute evidence for beneficial results in threatened abortion. And, the opinion that progestins have no effect in preventing abortion is prevalent among many clinicians. For example, a recent survey of Philadelphia obstetricians showed that 60% of those questioned about their attitudes toward treatment with progestins during pregnancy replied that they were convinced, by clinical experience, that the progestins had no value in threatened abortion; in spite of this conviction, 40% of the same group admitted prescribing progestins for such patients. At best, progestin is a questionable remedy for habitual or threatened abortion in man and its casual use in pregnant patients is generally unwarranted.

Adrenal Steroids

Because the adrenal corticoids, including cortisone and its many analogues, are rarely used in large doses during pregnancy, the incidence of related fetal damage is surprisingly low. In a review of 260 pregnancies during which corticoids were given for severe illness (such as lupus erythematosus), there were only a few cases of malformation (2 of cleft palate; one of temporary adrenocortical failure). It is difficult to assess the role of the corticoids on these infants because the serious maternal disease may it-

self have had an independent influence on fetal development. So, if we presume that the adrenal steroids are not used in large doses except for very compelling reasons, the possibility of fetal damage from their use appears to be small. As to the very small doses of corticoids such as are used in treating certain kinds of infertility—there are no reports to date of related fetal damage.

I would like to end this article with a plea for re-appraisal of the use of hormones during pregnancy. To be sure, if hormonal treatment brings forth an infant who might not otherwise survive, a correctable malformation is tolerable; if treatment is unnecessary, the risk of malformation is intolerable—however small it may be. So the use of hormones during pregnancy should be reserved for clear and compelling indications. This is true especially of the progestins whose therapeutic value has not been firmly established. Because the use of corticoids has been strictly limited during pregnancy, the number of fetal casualties attributable to these drugs has been surprisingly low. We would do well to exercise the same prudence in the use of estrogens and progestins.

In conclusion, I want to emphasize two obvious but sometimes overlooked principles: 1) Never use a potent drug during pregnancy unless the indication is clear; then, use the minimum effective dose. 2) If treatment involving a fetal hazard is necessary, keep in mind the anticipated effects so that any malformation can be recognized and corrected early.

LARYNGOLOGY

Raymond S. Rosedale, M.D.
Canton, Ohio

Raymond S. Rosedale is a member of the Senior Staff, Otolaryngology, and Chief of the Department of Plastic Surgery of the Head and Neck, Mercy Hospital and Timken-Mercy Hospital, Canton, Ohio. He is a Diplomate of both the American Board of Pathology (1937) and the American Board of Otolaryngology (1940). Included among his professional affiliations are the American Academy of Ophthalmology and Otolaryngology, International College of Surgeons, American College of Chest Physicians, and the American College of Allergists. In the May CONSULTANT, he wrote on hoarseness; this month he discusses indications for removing tonsils and adenoids.

TONSILS AND ADENOIDS—WHEN TO OPERATE

Although removal of tonsils and adenoids is probably the commonest operation done in the United States and the techniques are well defined, there still seems to be a great deal of uncertainty about when they should be removed—and when they should not.

There is a simple answer that everyone can agree on: they should be removed whenever local or systemic disease warrants their removal. But in that simple answer there is much room for disagreement and misunderstanding, so perhaps it could stand some expansion. These are the conditions I think make the operation mandatory:

1. Enlargement that interferes with swallowing or breathing.

2. Infections related to recurrent systemic disease, with exacerbations, such as pyelitis or rheumatic fever.

3. Repeated local infections that will not clear, such as staphylococcus or mixed infections with colds.

4. Chronic ear infections.

Chronic Nonspecific Infection

Chronic nonspecific tonsillitis presents a challenge to the clinician because of the lack of uniform diagnostic criteria. Nevertheless, because it is longitudinal diagnosis that is important, rather than the immediate appearance of the tonsils and adenoids, the clinician is in a position to make a sound decision.

A history suggesting a need for tonsillectomy is one of repeated attacks of tonsillitis, pharyngitis, or peritonsillar abscess, with progressive enlargement of the jugulodigastric lymph nodes. A history of foul breath, fatigability, and failure of growing children to gain weight may suggest consideration of tonsillectomy, but I would recommend detailed systemic examination first and treatment with vitamins and antibiotics before operation, in questionable cases.

In patients with chronic ear discharge and/or recurring hoarseness accompanying inflamed tonsils, tonsillectomy is recommended.

Focal Infection

The association of exacerbating tonsillitis with recurring pyelitis is well known, as is the relationship between rheumatic fever and tonsillitis; therefore these are indications for tonsillectomy. The relationship between tonsillitis and rheumatoid arthritis is not so clear, however. I would suggest a preliminary study for pathogenic bacteria in questionable cases.

Tonsillectomy is sometimes indicated in the treatment of bronchiectasis, when continuing evidence of tonsil infection coincides with stubborn cases, indicating infection may be spreading via connecting lymphatics.

Acute Infections with Inflammation

Although tonsillectomy has, on occasion, been recommended for treatment of certain instances of acute tonsillar infection and peritonsillar abscess, the principle does not seem rational to me. I prefer to manage acute inflammations conservatively by the use of hot saline irrigation, the ice collar, antibiotics, restorations of fluid balance, and topical analgesics.

Physical Diagnosis

The size of the tonsils, unless they interfere with swallowing, is of course not a major criterion for tonsillectomy. Nevertheless, I suspect that the factor of enlargement is still given too much weight in many diagnoses. Children's tonsils are often large, as is true of lymphoid structures generally before puberty. On the other hand, chronically infected tonsils in adults may not be enlarged.

Sometimes the very bulk of the tonsils interferes with swallowing, indicating a need for tonsillectomy. Since, like other lymphoid tissues, the tonsils tend to become smaller after puberty, persistent postpubescent enlargement may be viewed with suspicion, although even in adults large tonsils do not necessarily signify infection.

The degree of embedment in the pillars, the size, and the number of lacunae have nothing to do with chronic infection. The presence of white, yellow, or "cheesy" spots indicates only that the lacunae are filled with debris, and not necessarily that they are exudate. The debris may have originated in the nasal passages or sinuses and collected in the lacunae. Exudate tonsils, however, can be identified by applying pressure.

Sometimes a fine nodularity of the tonsil surfaces may be seen. This indicates lymphoid follicle hyperplasia. Scars rarely are seen on tonsils, but when they are, they may be regarded as stigmata of infected inflammation. Chronic hyperemia of pillars is prob-

ably one of the most reliable signs of chronic infection. Progressive enlargement of the jugulodigastric lymph nodes almost always occurs in chronic tonsillitis in children, but this is not so in adults. Increased leukocyte count and sedimentation rate, and fever often are not of primary importance in diagnosis.

Adenoids

In children, adenoidectomy and tonsillectomy usually are done together, but adenoid masses are seldom seen after puberty. Enlarged adenoids are associated with mouth breathing, languor, and the "adenoid facies." Primary adenoidectomy is indicated in chronic otorrhea and conduction deafness, when the adenoids are obstructive.

When Tonsils and Adenoids Should Not be Removed

Tonsillectomy and adenoidectomy should not be done for several weeks after acute tonsillitis, pharyngitis, or nasopharyngitis, nor too soon after the infectious diseases. Other contraindications are acute allergic states, and, of course, blood dyscrasias. In cleft palate patients, the tonsils are rarely removed because they aid in velopharyngeal closure to provide serviceable voice.

T & A and the Allergic Patient

Any trauma may touch off a latent allergy. This is especially true of tonsils and adenoid operations. In allergic children, respiratory allergy should be under control prior to the operation. Sometimes postoperative nasal allergy may be more troublesome to the patient than the previous adenoid disease.

Removing tonsils and adenoids may not necessarily improve an asthmatic condition and, to the contrary, may aggravate it; a primary attack of asthma may follow the operation. In considering whether removing tonsils and adenoids will reduce the incidence of colds in an individual, one must distinguish between "colds" and allergic upsets.

QUESTIONS AND ANSWERS

Q. *Should tonsils and adenoids be removed when neoplasms are present?*

A. Tumors and cysts warrant removal under certain circumstances, but each case should be decided specifically, preferably in consultation with a specialist. When a malignancy or potential malignancy is present, radical surgery or x-ray therapy, or both, will likely be needed.

Q. *Should tonsillectomy be postponed in a patient receiving polio immunization?*

A. There is a school of thought that holds tonsillectomy can be done if the patient has had four polio immunizations six months before the operation. It would seem prudent, however, not to operate during the time the disease is common in the community.

PARNATE®

brand of tranylcypromine

relieves depression

- faster onset of action than any previously available antidepressant with similar indirect action
- specific antidepressant effect—relieves such primary symptoms as dejected mood, inactivity and inability to concentrate
- a new monoamine oxidase inhibitor—unrelated chemically to the hydrazine antidepressants
- convenient b.i.d. dosage

AVAILABLE: 'Parnate' Tablets, 10 mg., in bottles of 50. Each tablet contains 10 mg. of tranylcypromine (trans-*dl*-2-phenylcyclopropylamine) as the sulfate.

For complete prescribing information, see back of magazine.

SK&F leaders in psychopharmaceutical research

STELAZINE®

brand of trifluoperazine

relieves anxiety

- therapeutic response often within 24 to 48 hours
- specific antianxiety effect—relieves such symptoms as agitation and tension
- infrequent side effects—when they do occur, they are usually mild and transitory
- convenient b.i.d. dosage

AVAILABLE: 'Stelazine' Tablets, 1 mg. and 2 mg., in bottles of 50. Each tablet contains 1 mg. or 2 mg. of trifluoperazine, as the dihydrochloride.

For complete prescribing information, see back of magazine.

SK&F leaders in psychopharmaceutical research

GYNECOLOGY

J. Ernest Ayre, M.D.
Cancer Cytology Foundation of America

J. Ernest Ayre is Medical and Scientific Director of the Cancer Cytology Foundation of America. Before assuming this position, he served as director of McGill University's Cytology Research Laboratory, as director of the Cancer Institute at Miami, and as founding president of the Pan-American Cancer Cytology Society. He is a Diplomate in Gynecology of the Royal College of Surgeons of Canada. In the July issue of CONSULTANT, Dr. Ayre discussed the importance of and the technique for office diagnosis of cervical cancer. Now he turns his attention to endometrial cancer.

DETECTING ENDOMETRIAL CANCER BY A SIMPLIFIED OFFICE TECHNIQUE

Television producers are said to have a motto: "If at first you succeed, try, try again." Certainly cytologists reason the same way. If by simply examining cells scraped from the cervix you can succeed in diagnosing very early cervical cancer, and if the technique proves so reliable that it seems likely to eliminate cervical cancer as a major cause of death, why not try, try again? Why not attack cancer at other sites – for instance, cancer of the endometrium – the same way?

Readers of CONSULTANT are familiar with the cytologic technique for detecting cervical cancer; it was described in the July issue. It is simple and sure and hence should be a part of the routine office examination of every woman over 20. Incidentally, cervical cytology alone will detect 65 to 70% of all endometrial cancer. But can cytologic techniques be applied for detecting endometrial cancer directly? The answer is yes, but the problem is a little more difficult and its solution not quite so pat.

Obtaining cells from the endometrium is not quite as easy as obtaining cells from the cervix. The endometrium is less accessible, especially since stenosis and, sometimes, occlusion of the endo-cervical canal occur frequently in women at the age when they are most prone to endometrial cancer. In contrast to cervical cancer, endometrial cancer is rarely seen in women under 40; it develops most frequently between the ages of 45 and 65.

The problem of collecting samples of cells representative of the whole endometrium at first proved difficult; false negatives were reported in 20-

30% of all cases of endometrial cancer. Now, however, new aspiration and brushing techniques have cut the error to as low as 5%. But before describing these techniques, let us pose one other question.

Who Should Be Tested?

Should endometrial smears be recommended for every menopausal woman with or without symptoms? Or should we test only those who we suspect have cancer? So far, there is insufficient data to answer with confidence. However, I believe the technique to be described is sufficiently safe, accurate, and economical to be used as a routine screening test for all menopausal and postmenopausal women. In fact, it is now sufficiently precise to diagnose such borderline malignancy as carcinoma *in situ*. By emphasizing its value as a screening test, I do not mean to belittle its importance in diagnosing suspected malignancy. Here, too, the technique proves extremely valuable.

How It Is Done

The technique that I prefer for obtaining the endometrial sample makes use of a plastic, disposable brush. Aspiration of the cells from the uterus with a cannula is also satisfactory, but in my experience, a third method, the lavage technique, is not as reliable.

Routine cancer cytologic studies begin with a cervical smear (see CONSULTANT July 1961, page 42). This not only rules out cervical cancer but also provides an important clue for the cytologist attempting to interpret borderline changes in endometrial cells. With an abnormal endometrial smear, abnormally high estrogenic cornification of the cervical cells is a contributing sign of malignancy. After obtaining the cervical smear, sterilize the cervix and endometrial canal with tincture of Zephiran. Then grasp the cervix gently with a tenaculum or Allis clamp. To avoid discomfort, apply pressure slowly and avoid pulling the cervix vigorously.

Frequently the cervix will be sufficiently open to receive the small-caliber endometrial brush-tube, but usually it is advisable to first gently pass a sterile probe and then a #1 Hegar dilator through the cervical os to stretch it. Next insert the sterile plastic tube of the endometrial brush about 6 to 10 cm. into the uterus. The tube is flexible, so there is little chance of rupturing the uterine wall. Even so, never use strong pressure; it is possible that a paper-thin, senile uterus or a uterus made fragile by extensive malignancy might be perforated. However, I have very rarely seen evidence of perforation in thousands of cases.

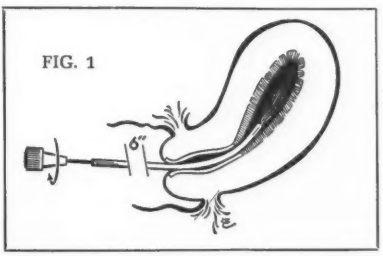


FIG. 1

Once past the internal os, push the plastic tube 2 to 4 cm. further. Then extrude the brush, and rotate it several times to sweep the walls of the cavity (Figure 1). Then draw the brush back into the plastic tube, so that its rich sample of cells is protected by the plastic sheath as the brush is withdrawn from the uterus. Once removed from the vagina, again extrude the brush and place it upon a glass slide.

With a second slide, gently push the cells and secretion from the bristles onto the first slide. Label the sample to differentiate it from the one obtained from the cervix, and fix it in a 50-50 solution of ether and 95% alcohol solution for 30 to 60 minutes.

To prepare the slides for mailing, place a drop of glycerine upon the smear and place a second slide over the first. Wrap the two together and send them with the patient's history to the cytology laboratory just as you would a cervical smear.

QUESTIONS AND ANSWERS

Q. *Where can the disposable endometrial brush be purchased?*

A. The Adams brush described in this paper is manufactured by the Clay-Adams Company, 141 East 25th St., New York City.

Q. *Does the brush technique have any application in women under 40?*

A. Although uncommon, endometrial cancer does occur in women under 40, so the brush technique should be used to rule out endometrial cancer whenever the cervical smear is suspicious or when abnormal bleeding is present.

Q. *Is there a risk of disturbing early pregnancy with the endometrial brush?*

A. Any object placed in the uterus of a premenopausal woman might cause abortion of an early pregnancy. The Friedman pregnancy test or scheduling the examination soon after menstruation would reduce the risk.

Q. *Is confirmation by curettage needed after a positive cytodiagnosis?*

A. When the cytologist or pathologist reports that a smear obtained by endometrial brush is conclusive for cancer (as in Figure 2), the diagnosis is as reliable as one based on curettings. Curettage, with its risk of spreading cancer cells, is then unnecessary. Of course, when the smear is interpreted as merely suspicious, confirmation by curettage is necessary.

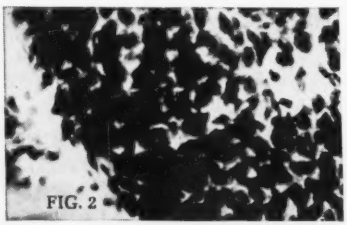


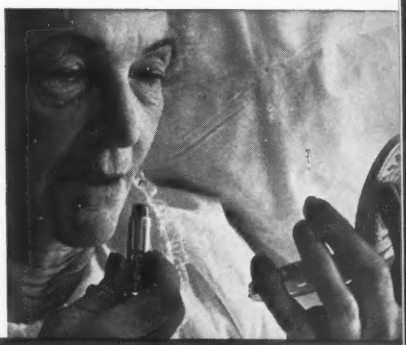
FIG. 2

Q. *Without a nearby cytology laboratory, how can reliable interpretation of cytology smears be obtained?*

A. Smears can be mailed to a laboratory that specializes in cytodiagnosis. Lists of mail-order laboratories are available from the Cancer Cytology Foundation of America, 115 East 69th St., New York 21, N. Y. Technical booklets and free cytology kits are also available on request.

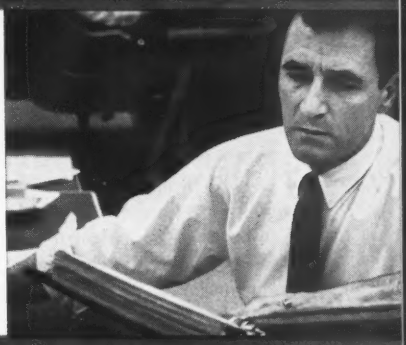
THANKS TO THEIR DOCTOR— and THORAZINE®

brand of chlorpromazine



this cancer patient's suffering is eased

- her high narcotic dosage has been markedly reduced
- her mental outlook has noticeably improved
- before her doctor came she asked her nurse for her lipstick



this alcoholic is back on the job

- his agitation is under control
- his craving for alcohol is on the wane
- his doctor's advice is now welcome and heeded

this surgical patient wanted steak for breakfast

Despite major surgery less than 48 hours ago:

- her nausea is almost completely relieved and her appetite is near normal
- her pain and suffering are well controlled
- she has asked her doctor how soon she can go home

Though the photographs above were professionally posed, they faithfully reflect case histories that are brought to our attention almost daily—histories that explain the widespread acceptance of 'Thorazine' (brand of chlorpromazine) as a fundamental drug in both office and hospital practice.

SK&F Smith Kline & French Laboratories, Philadelphia

For complete prescribing information, see back of magazine.

PEDIATRICS

Susan C. Dees, M.D.
Duke University

Susan Dees is Professor of Pediatrics in Allergy at Duke University in Durham, North Carolina. A Fellow of the American Academy of Pediatrics, the American College of Allergists, and the American Academy of Allergy, she is a Past-President of the North Carolina Pediatric Society and currently serves as President of the Southeastern Allergy Association. Her investigative work has dealt chiefly with the problems of allergy in children and has been published in 42 articles in various scientific journals.

THE PUZZLES OF FOOD ALLERGY

I have to begin by saying that I cannot write a practical article on food allergies—one that will nicely lay out what to look for and what to look out for. I wish I could; I wish there were three simple rules to follow, or five foods to avoid, or seven things to do to solve the problem of food allergies in children. But there aren't. There are only puzzles. However, just knowing what these puzzles are can be a big help in understanding the inconsistencies in the tests for food sensitivity, and that understanding, in turn, can lead to better care for our patients.

Etiology

We have no ready explanation for the why and how of food allergy. We all know people who regularly develop one of the typical allergic reactions of hives, asthma, rhinitis, or eczema after eating certain foods. We see infants, children and older people with the whole gamut of gastrointestinal symptoms after a meal containing some food to which they are allergic. Allergy to food has been recognized since antiquity, and its existence so commonly accepted that there are no accurate figures on its incidence.

Some of the puzzling aspects of food allergy arise from the fundamental enigma of all allergic reactions: why do they arise in the first place? Is it because some people are more easily sensitized than others, or because certain foods are very potent allergens? Evidence that an allergic constitution or diathesis exists comes from certain families in whom allergy appears to be genetically determined. In such families, medical records show generations of allergic persons. However, subtle individual differences must also be decisive factors in both the process of sensitization and its clinical expression. We have studied identical twins

whose allergies varied both in degree, in age of onset, in systems involved, and in the particular foods to which they were sensitive. We also see other persons who develop exquisite or multiple sensitivity to foods, and who know of no allergic ancestors.

Part of the explanation for allergy may reside in the chemical nature of certain foods and substances known to be lively allergens. For example, eggs, shellfish, nuts, and other edible seeds commonly provoke severe sensitization; they usually give strongly positive immediate skin tests that correlate highly with acute clinical food allergy. (Example: the infant whose lips and eyes swell shut with a taste of egg-white meringue, and who gives a 4+ positive scratch test reaction to egg white.)

These foods—the known sensitizers—and their effects in animals and humans have been widely studied in an attempt to understand the process of sensitization. So far, these investigations have produced more questions than answers and the process of sensitization is only dimly understood. We know that protein or molecularly protein-like substances cross the gastrointestinal wall into the blood stream where they appear as potential allergens. We know, too, that very young infants, children with diarrhea and other illnesses, and certain adults absorb these antigens easily. We do not know the site of antibody formation; it may be in the bowel wall, or in some distant site, and may even vary at times in the same person.

Paradoxically, both a rise and a decline in antibody titers to ingested and injected food allergens have resulted from repeated planned exposure. These results confirm the clinically familiar reports from patients of a childhood food sensitivity that has disappeared for no apparent reason. We also hear exactly the opposite story from oldsters who find themselves allergic to foods they once ate with relish and without trouble. We have no explanation for this variability in development of allergy. We have only the observation that repeated contact with an allergen may eventually result in tolerance or desensitization; under other circumstances, when the exposure and timing are just right, repeated contact may result in heightened sensitivity.

Perhaps the best known of the allergy tests is the direct skin test, which gives an immediate wheal-erythema reaction when an antigen is scratched, pricked, or injected into the skin of a sensitive person. Another familiar test is the indirect passive transfer test, which utilizes the peculiar affinity of the circulating antibodies for skin cells. In the original test, serum containing fish antibody was injected into the skin of the recipient who subsequently ate fish and reacted with immediate itching wheal-erythema at the sensitized site.

These tests have been useful in the attempts to define allergy, but have themselves given rise to puzzling situations. For example, the immediate skin test may be negative in a person with definite clinical sensitivity to a food, or positive in a person with no clinical sensitivity. Moreover, the skin test for *intact* food may be negative in some patients in whom symptoms do not follow immediately after eating the food, while the proteoses or partially digested products of the same food may produce both symptoms

and positive skin tests. This probably occurs frequently, but we will not know how frequently as long as the passage of a gastric tube is the only way to recover the offending allergen.

There are many factors that may alter or affect reactions to foods once they enter the gastrointestinal tract. The gastrointestinal environment may vary widely in the same person according to his physiologic function at any given time. For example, the emotions may cause changes in the amount and composition of salivary, gastric, and intestinal secretions; this will affect the enzyme content, the acidity, and alkalinity to which the food is exposed, and affect its rate of digestion as well as the products formed. Emotional factors, as well as the pH of the gut, and the type of food ingested also affect the motility of the various parts of the gastrointestinal tract; thus the duration of exposure to digestive juices may be quite variable and influence the stage of digestion at which food is absorbed.

Our studies on allergy to alcoholic beverages further illustrate the effect on allergic reactions of substances other than the food allergen itself. We found that the presence of alcohol in the stomach increased both the size of the positive skin test and the rate at which it appeared. In persons clinically sensitive to a food, symptoms appeared more quickly and tended to be more severe if the food had been taken either with or shortly after ingestion of alcohol.

Another factor to keep in mind with regard to skin testing is that extracts of certain foods are naturally irritating and will give positive skin tests in practically everyone tested. Such non-specific reactors include spinach, white potato, tomato, banana, citrus fruits and certain spices; they seem to be equally irritating to non-allergic and allergic skins, but seem to cause real allergy infrequently.

These various and variable reactions to skin testing with food allergens are probably the most bewildering aspect of the clinical diagnosis of food allergy. They have led many people to say, "I do not believe in skin tests or in allergy." Still other problems arise in deciding which of many foods are responsible for a patient's allergic symptoms. The most common error in this area is not realizing that foods in their table form are complex substances. Commercially prepared foods often contain many ingredients in addition to the major one. These "hidden ingredients" rather than the major one may be the active allergen. We must also remember that the seasonings, the preservatives, may be potential allergens. Such things as vegetable gums used as stabilizers, and antibiotics such as penicillin in milk or aureomycin in poultry and seafood may prove to be the actual allergens.

Can these puzzles of food allergy serve any practical purpose other than to stimulate us to search harder for the answers? If we can constantly remember that a food allergen may not always be the same every time it is eaten, and the allergic person's physiologic state may be very different at different exposures, this may make us more critical in our evaluation of food allergy. It should give us a more workable approach to our objective tests for food sensitivity, and let us interpret any inconsistencies between them and the clinical history more intelligently.

QUESTIONS AND ANSWERS

Q. *What is the usual procedure for dealing with an allergic infant?*

A. Under 6 months of age, foods are the most likely allergens. Find out which foods are being used, and whether any cause observable symptoms. Eliminate a suspicious food from the diet and substitute a nutritionally equivalent food, for a period of at least one week. Then reintroduce the food or foods one at a time at intervals not oftener than every 2–4 days. Observe the child for any recurrence of trouble. Unless producing symptoms would be hazardous to the child, repeat this trial at least 3 times at intervals of several weeks before assuming that a particular food is the cause of the allergy.

Once a food allergen is identified positively, it should be avoided for a minimum of several months. When satisfactory improvement has occurred, the food may be returned to the diet, either gradually, or in normally used amounts, depending on individual situations. Frequently this period of abstinence will result in renewed tolerance for the food. All allergic infants should be fed simple diets, avoiding mixtures of foods until each food is known to be well tolerated. Egg should not be used before 6 months of age, and preferably not before 1 year.

In older infants and young children, airborne as well as food allergens may be responsible for symptoms, so, the prevention of exposure to these inhalants or desensitization to them are necessary in addition to diet control.

Q. *Are antihistamines and steroids useful in treating food allergy?*

A. Antihistamines are less effective in food allergy which causes gastrointestinal symptoms, than that which causes allergic rhinitis or hives. Steroids are useful when allergic symptoms are severe or prolonged. However, steroids taken before eating a food allergen will not prevent an allergic reaction to the food.

Q. *Can a child be desensitized to a food?*

A. The injection method is ordinarily not practical. The oral method of feeding minute amounts, increased gradually over many weeks or months is often effective in desensitizing very sensitive persons who cannot completely avoid a food.

Q. *How common is cow's milk allergy in children? And how is it treated?*

A. We found 1% of a series of 400 unselected well babies clinically sensitive to cow's milk. Cow's milk allergy is treated by using a milk substitute formula.

Several very satisfactory commercial products made from Soybean, amino acids or strained meat are available. Breast feeding is the best way to prevent development of cow's milk allergy.

for a brighter pregnancy

DEXAMYL® SPANSULE®

brand of sustained release capsules

When pregnancy becomes burdensome, 'Dexamyl' Spansule capsules can help restore optimism and drive.

FORMULA: Each 'Dexamyl' *Spansule* capsule No. 1 contains Dexedrine® (brand of dextro amphetamine sulfate), 10 mg.; amobarbital (Warning, may be habit forming), 1 gr. Each 'Dexamyl' *Spansule* capsule No. 2 contains 'Dexedrine' (brand of dextro amphetamine sulfate), 15 mg.; amobarbital (Warning, may be habit forming), 1½ gr. The active ingredients of the 'Spansule' capsule are distributed among hundreds of minute pellets with varying disintegration times. A therapeutic dose is released immediately and the remaining medication, released slowly and without interruption, sustains the effect for 10 to 12 hours.

INDICATIONS: (1) Mental and emotional distress; (2) overweight.

SIDE EFFECTS: Insomnia, excitability and increased motor activity are infrequent and ordinarily mild.

CAUTIONS: Should be used with caution in patients hypersensitive to sympathomimetic compounds or barbiturates and in cases of coronary or cardiovascular disease or severe hypertension.

ALSO AVAILABLE: 'Dexamyl' Tablets and Elixir.

Prescribing information adopted January 1961.

Smith Kline & French Laboratories, Philadelphia SK&F

HEMATOLOGY

Virgil Loeb, Jr.
Washington University

Virgil Loeb, Jr., is Assistant Professor of Clinical Medicine and Pathology at Washington University School of Medicine, St. Louis. He is also Director of the Central Diagnostic Laboratories at Barnes Hospital and Chairman of the Medical Advisory Committee, St. Louis Regional Blood Program, American Red Cross. Dr. Loeb has participated as a panel member on several SK&F Medical Color Television programs on hematology. His professional affiliations include the International Society of Hematology and the American College of Physicians.

THE HAZARDS OF TRANSFUSION THERAPY

Each year in the United States, approximately 4,500,000 pints of blood are transfused to over 2,000,000 patients. In a recent study of transfusion practices in a major medical center, it was concluded that at least one-third and perhaps as many as three-quarters of the single unit transfusions given on the surgical service were unnecessary. I believe that the number of transfusions would drop significantly if all physicians were as well acquainted with the *hazards* of blood transfusions as they are with the benefits.

Transfusion Benefits

Modern blood banking techniques and facilities have provided the physician with a ready supply of safely stored whole blood and separated components such as packed red cells, whole plasma, and fractionated plasma proteins. As a result of this, additional methods of therapy have been made available to the physician. For example, administration of packed red cells from which plasma has been removed is vital for patients who need these cells but whose circulatory system is overloaded. The infusion of whole plasma, stored under proper conditions, is extremely valuable for expanding blood volume. And so is fresh-frozen plasma in the management of patients with certain coagulation defects. Protein fractions such as fibrinogen, albumin, and gamma globulin are also available and highly

useful to physicians for a variety of indications.

Indications for Therapy

It has been said that the five most important occasions when transfusion therapy should be considered are: (1) to maintain blood volume and prevent or treat shock, (2) to maintain the oxygen-carrying capacity of the blood and to prevent or treat acute hypoxia, (3) to promote or maintain coagulation of the blood, (4) for exchange transfusions in the newborn infant and (5) to maintain the circulation, as in extracorporeal or cardiac-bypass shunts.

Transfusion Hazards

Before deciding on transfusion therapy, however, each physician should weigh the possible hazards that may be involved against the benefits of such therapy. I think the indiscriminate use of "elective transfusions"—a term to cover the multiplicity of circumstances where transfusions are prescribed, but for which the indications have not been conservatively evaluated—and the frequent practice of giving the patient just a single pint of blood should be discouraged. What are the most important hazards of transfusion therapy to be anticipated? The main ones are circulatory failure, hemolytic transfusion reactions, other types of transfusion reactions, serum hepatitis, excessive iron deposition in tissues, and the development of transfusion polycythemia. Each of these hazards could lead to severe complications.

Some physicians fail to consider that a cyanotic patient with a weak cardiac reserve can be thrown into *circulatory failure* by transfusion of whole blood. While the patient may require red cell replacement, his circulatory system may be overloaded by the added plasma. Frequent measurement of the venous pressure during the administration of blood to an elderly patient with severe anemia and heart disease will often warn the physician of impending circulatory overload.

The common denominator in all *hemolytic transfusion reactions* consists of incompatibility between the donor and the recipient's blood group. Either the donor's erythrocytes may be hemolyzed by antibodies in the recipient's plasma or the recipient's red cells may be destroyed by antibodies passively transferred in the donor's plasma. No longer can an individual be classified as belonging simply to certain ABO and Rh groups. At least nine major blood groups are well established and many more minor blood groups have been recognized. With the blood group antigens identified at the present time, the number of theoretically possible different blood group phenotypes is over 500 billion. So it is obvious that "completely compatible" transfusions between donor and recipient are impossible. Fortunately, however, although minor blood group incompatibilities cannot be prevented, serologic techniques are available that will diminish greatly the possibility of reactions occurring as the result of the presence of pre-existing antibodies in either the donor or the patient. Essentially, all transfusions are potentially sensitizing ones. With proper blood banking technique, however, it is reasonable to say that incompatible hemolytic transfusion reactions are wholly preventable and are inexcusable when they do occur.

Other types of transfusion reactions take the form of fever, chills, bleeding, urticaria, and, occasionally, death from bacterial endotoxin present in contaminated donor units. Even though it appears to be perfectly normal when inspected prior to infusion, improperly stored or collected blood may be contaminated with organisms that can cause death. Also, recipients may become sensitized to the platelets or leukocytes in the donor blood, in which case subsequent transfusions may cause deleterious consequences.

Serum hepatitis may develop in a recipient as a result of the presence of the virus in any transfused material. Fortunately, the problem of transmission of hepatitis following the administration of pooled plasma seems to have been successfully reduced by the prior storage of such plasma at 32°C. for a period of six months, but it must be emphasized that this disease may be transmitted by any blood component not free from virus.

Transfusion hemosiderosis, the deposition of abnormal amounts of iron in tissues, often results from multiple transfusions. Unfortunately, it may be unavoidable since many patients with bone marrow failure depend upon transfused blood to live, being unable to manufacture their own red cells. However, in other cases, excessive transfusions may easily overload the body's iron stores with attendant hepatic and cardiac complications.

Transfusion polycythemia may occur in the patient who has been given a so-called tonic or "cosmetic" transfusion, which makes his physician feel better, but has an adverse effect on the patient. That is why it ought to be an edict that when a physician feels his patient needs just a single transfusion as part of the medical management of his disease, he probably should not get any at all. Exceptions to this rule are uncommon. The injudicious use of whole blood or its components in transfusion therapy is fraught with danger. Patients with far advanced malignant diseases do not require levels of hemoglobin comparable to those of the healthy individual. The masking of an underlying anemia by transfused blood may obscure the clinical problem and make accurate diagnosis difficult, if not nearly impossible. Deficiencies of vitamin B_{12}, folic acid, or iron should be treated physiologically with replacement of the proper factor, rather than with whole blood.

Two other possible consequences worth mentioning, are: (1) the production of isosensitization where a patient develops antibodies that make future transfusions or pregnancies complicated, and (2) delayed convalescence due to the depressing effect of transfusions upon normal red blood cell production by the bone marrow.

Inescapably, it is the clinician's responsibility to decide whether or not blood is to be given. He must be aware of all the hazards and problems involved in making the decision. As Crosby[1] has recently stated: "Thoughtless prescription of blood transfusion is playing Russian roulette with bottles of blood instead of a revolver. While the odds are in the physician's favor that nothing will go wrong, the patient takes the risk."

1. Crosby, W. H. "Misuse of Blood Transfusions," *Blood*, vol. 13, pp. 1198-1200, 1958.

Without question
the standard drug for weight reduction

is widely accepted, superbly documented 'Dexedrine'. Because it not only controls appetite but also encourages mental and physical activity, 'Dexedrine' renews the patient's interest in life, reduces her chronic and frequently morbid yearning for food.

DEXEDRINE® *Smith Kline & French Laboratories, Philadelphia*

brand of dextro amphetamine

Formula—Each 'Dexedrine' Tablet contains dextro amphetamine sulfate, 5 mg. **Indications**—For the control of appetite in weight reduction, depressive states, alcoholism, narcolepsy. **Dosage**—For weight control, up to 30 mg. daily, in doses of 5 to 10 mg., 30 to 60 minutes before meals. For depressive states and alcoholism: up to 30 mg. daily in doses of 5 to 10 mg. at intervals of 4 to 6 hours. For narcolepsy: up to 50 mg. daily. **Side effects**—insomnia, excitability and increased motor activity—are infrequent and ordinarily mild. **Cautions**—Use 'Dexedrine' with caution in patients hypersensitive to sympathomimetics, in coronary or cardiovascular disease, in severe hypertension. **Contraindications**—Agitated pre-psychotic states and hyperexcitability. **Available**—5 mg. tablets, in bottles of 100.

Prescribing information adopted January, 1961.

SPECIAL FEATURE

Lester W. Burket, D.D.S., M.D.
University of Pennsylvania

Lester W. Burket is Dean of the School of Dentistry and Professor of Oral Medicine at the School of Dentistry and Graduate School of Medicine, University of Pennsylvania. He is currently President of the American Association of Dental Schools, and a member of the Council on Dental Education of the American Dental Association. Dr. Burket is especially interested in improving cooperation between medicine and dentistry, and has also been active in research on the systemic significance of oral foci of infection. He is author of the text ORAL MEDICINE: DIAGNOSIS AND TREATMENT (Lippincott).

WHAT DENTISTS NEED TO KNOW ABOUT YOUR PATIENTS

I would like to see better cooperation between physicians and dentists. For one thing, the fact that patients visit their dentists regularly for checkups gives the dentist a unique opportunity to recognize changes in the patient's general health and to detect unsuspected systemic diseases that have oral manifestations. For another—and one which I want to highlight in this paper—physicians administer drugs which may significantly modify the dental treatment. If, for example, the patient is receiving an anticoagulant, corticosteroid, or potent antihypertensive drug, certain precautions are necessary to minimize the possibility of complications following dental extractions or soft-tissue-manipulative procedures. With the widespread use of potent and potentially dangerous drugs for many chronic diseases, it is particularly important that your patient's dentist know what medications the patient is receiving. You can help to assure proper treatment by remembering the following points.

Rheumatic Heart Disease

Almost all physicians know the potential hazards of transient bacteremias in persons with a history of rheumatic or congenital heart disease. The American Heart Association and the Council on Dental Therapeutics of the American Dental Association have made joint recommendations for prophylactic antibiotic therapy in such patients before surgical or manipulative procedures on the oral structures. Thus, if your patient has a history of rheumatic or congenital

heart disease, you should instruct him to inform his dentist about it.

Post-Coronary Thrombosis

Long-term anticoagulant therapy is now widely used in ambulatory patients following coronary occlusion, arterial thrombosis, and thrombophlebitis. Such patients may seek dental consultation for treatment of "bleeding gums," if the physician prescribing this medication does not mention this possible side effect. At times, the usual treatment for gingival irritation —scaling of the teeth and curettage of the adjacent gingival tissues—has resulted in severe hemorrhage in patients receiving anticoagulants—hemorrhage which is both alarming to the patient and difficult for the dentist to control. Even when a history of drug medication is taken by the dentist, the patient may not volunteer the desired information because the prescribing physician did not stress the importance of telling the dentist about it.

Patients receiving anticoagulant therapy who require dental extractions or gingival curettage or surgery present a problem that requires cooperation of the dentist and the physician. The possibility of temporarily withholding the anticoagulant drug is a decision which should be made only by the physician. If the physician feels that anticoagulant therapy must be continued, then the dentist will have to be prepared to cope with the possibility of abnormal bleeding, and the surgical procedures, if extensive, should be performed in the hospital. Recently, several reports have indicated that by following special surgical procedures, anticoagulant therapy may be continued at a somewhat lower level during oral surgery. It is of utmost importance, however, that you tell the patient to inform the dentist about anticoagulant therapy.

Hypertensive Heart Disease

A large number of antihypertensive agents are now available and are being extensively used. A relatively common side reaction of these drugs is nausea and vomiting. This reaction is especially likely to occur when impressions are being taken for full dentures or when full-mouth roentgenograms are being exposed. The stress associated with dental operative procedures also tends to precipitate these reactions.

Moreover, in patients receiving antihypertensive drugs, sudden changes in posture, as when the patient quickly arises from a partially reclining position in a dental chair, may result in marked hypotension and syncope. Patients receiving these drugs, especially Rauwolfia derivatives, may develop profound circulatory depression during surgery. This profound drop in blood pressure cannot be corrected by epinephrine administration and, hence, if the dentist were to use epinephrine instead of neosynephrine or levarterenol, would only aggravate the circulatory collapse. The antihypertensive drugs also have varying degrees of sedative effect, and they may potentiate sedation with barbiturates used as dental preoperative medication. Hence, it is extremely important that you tell patients who are taking antihypertensive agents to inform the dentist about the type of medication being used, so that he can reduce the usual dose of dental preoperative medication.

Chronic Passive Congestion or Cardiac Decompensation

The mercurial diuretics whether given by injection, suppository, or by mouth, may produce an acute form of ulceronecrotic stomatitis. Patients with this complication would naturally consult the dentist first. The usual dental treatment will be ineffective unless the mercurial drug is stopped. Non-mercurial diuretics are now being more extensively used. At least one, Diamox, is known to sometimes result in oral lesions similar to ulceronecrotic gingivostomatitis (Vincent's) and, rarely, facial paresthesia. These patients will also likely consult the dentist first for the treatment of the painful oral lesions. Whenever you prescribe this group of drugs, it is desirable to tell the patient about possible oral side effects, so that cooperative care by the dentist can achieve a satisfactory result.

Allergic Conditions

A wide variety of drugs are used for the treatment of allergic conditions. Many of them produce drowsiness. The prolonged administration of these drugs may also produce considerable central depression of the nervous system, hence the dentist may find it desirable to reduce, or possibly eliminate, the usual preoperative medication with barbiturates. A rare side effect of some of the antihistamines is severe depression of the leukocytes with the development of malignant neutropenia, which may be first evidenced by ulceronecrotic lesions of the gingival, pharyngeal and buccal mucosa.

Diabetes

Patients with diabetes are generally well informed by their physician about the need for optimum health of the oral tissues and the elimination of infections anywhere in the body. Additional attention should be paid to educating diabetic patients to inform their dentist of their diabetic condition. This will enable the dentist to place the patient on a home and office regimen which will minimize the development of infections of the teeth or soft oral tissues and also allow better control of the diabetic state. The dentist will usually consult with the patient's physician about the type of anesthetic to be used when oral surgical procedures are contemplated and whether prophylactic antibiotic therapy may be desirable.

Addison's Disease and Corticosteroids

More and more patients are receiving one of the corticosteroid preparations for various disease states. These agents depress the natural defensive mechanisms of the body such as inflammation. As a result, early and characteristic signs and symptoms of oral diseases may be supressed, or at least greatly modified, thus complicating diagnosis. At times, a paradoxical effect follows corticosteroid therapy with the development of ecchymotic areas which may be observed first in the oral cavity. These occur more frequently with prednisolone.

Patients with Addison's disease should be warned that an adjustment in cortisone or corticosteroid dosage may be required prior to dental surgical procedures. These patients should have the surgical procedures performed in a hospital, where complications or a "crisis" can be treated best.

Since the corticosteroid drugs suppress the defensive reactions of the body to injury, postoperative infec-

tions are more likely to occur following dental extractions or surgery of the soft oral tissues. For this reason, prophylactic antibiotic therapy is usually indicated before and after the surgical procedure in patients receiving corticosteroid therapy systemically. Since some modification of the usual dosage of the corticosteroids by the physician may be desirable to accommodate for the added stress associated with the surgery, dentist-physician consultation is highly desirable.

There are few, if any, dental indications for use of the corticosteroids except for the treatment of the oral lesions of dermatologic conditions such as pemphigus and erythema multiforme. The topical use of corticosteroid preparations for nonspecific inflammatory conditions or the oral mucosa is not recommended, because the treatment is only symptomatic, and because the anti-inflammatory agents may cause delay in arriving at a correct diagnosis, or may mask the progress of disease.

Central Nervous System Depressants

A large number of drugs, especially the barbiturates and ataractics, are used for continued sedation in patients with epilepsy, hyperthyroid states, Parkinson's disease, and at times dysmenorrhea. Because these patients are already in a state of partial sedation, the administration of the usual dosage of dental preoperative sedation may be hazardous. Also if preoperative medication is used, the same precautions listed for the patients receiving antihistamines should be taken in respect to driving automobiles and having a responsible person accompany the patient following dental treatment.

in "morning sickness"
keep her spirits up...
and her breakfast down

Compazine® Spansule®

brand of prochlorperazine — brand of sustained release capsules

To keep her spirits up—One 'Compazine' *Spansule* capsule on arising provides a daylong calming effect that helps to keep your patient on an even emotional keel. Anxiety and irritability are controlled, yet your patient stays alert.

To keep her breakfast down—One 'Compazine' *Spansule* capsule at bedtime provides antiemetic action that lasts throughout the night and into the morning—thus protecting against "morning sickness."

15 mg. capsule—ideal for once-a-day administration
10 mg. capsule—ideal for twice-a-day (q12h) administration

In labor and delivery—'Compazine' Injection is particularly useful to relieve anxiety or to control nausea and vomiting.

For complete prescribing information, see back of magazine.

Smith Kline & French Laboratories, Philadelphia SK&F

THORAZINE®
brand of chlorpromazine

PRESCRIBING INFORMATION

Tranquilizer • Antiemetic • Potentiator

The wide diversity of clinical applications in which 'Thorazine' is valuable, as either a specific or an adjuvant, is due to its three fundamental clinical properties: (1) its capacity to alleviate anxiety, tension and agitation without dulling mental acuity, (2) its ability to potentiate sedatives, narcotics and anesthetics, and (3) its profound antiemetic effect.

The tranquilizing effect of 'Thorazine' accounts for its usefulness in somatic conditions where emotional stress is a factor, as well as in mental and emotional disturbances *per se*.

INDICATIONS

The value of 'Thorazine' is established in the following conditions:

Moderate to severe mental and emotional disturbances of everyday practice, particularly those disturbances marked by agitation, tension, apprehension, excitement, or anxiety.

Somatic conditions complicated by emotional stress, such as arthritis, tuberculosis, severe tension headaches, gastrointestinal disorders, dermatologic conditions, status asthmaticus and severe asthma.

Hospitalized psychiatric patients, to control agitation, dispel delusions and hallucinations, and at the same time to restore or increase the patient's capacity to respond to psychotherapy.

Nausea, vomiting and hiccups, with dramatic results in severe and refractory cases.

Acute or chronic alcoholism, to control agitation, delirium tremens, and nausea and vomiting.

Cancer, as an adjuvant, to control apprehension, suffering due to pain, and nausea and vomiting.

Intractable pain, to reduce suffering and to potentiate narcotics or sedatives.

Obstetrics, as an adjuvant, to control apprehension, pain, and nausea and vomiting. 'Thorazine' allows a reduction in the amounts of the drugs ordinarily used in obstetrical management, thus lessening the risk of respiratory depression in mother and infant.

Surgery, as an adjuvant, to control anxiety and apprehension, pain, and nausea and vomiting; and to reduce by potentiation the amounts of narcotics, sedatives and anesthetics needed.

ADULT DOSAGE AND ADMINISTRATION

Dosage should always be adjusted to the response of the individual and the severity of the condition. It is important to increase dosage until symptoms are controlled or side effects become troublesome.

Mental and Emotional Disturbances of Everyday Practice – Depending on severity, *starting oral dosage* is 10 mg. t.i.d. or q.i.d., or 25 mg. b.i.d. or t.i.d. After a day or two, dosage may be increased by increments of 20 mg. to 50 mg. daily, at semiweekly intervals (increase should be more gradual in emaciated or senile patients) until achieving maximum clinical response. Continue dosage at this level for at least two weeks; then it can usually be reduced to a maintenance level. A daily dosage of 200 mg. is "average," but in some cases, such as discharged mental patients, daily dosages as high as 800 mg. may be necessary. *Starting intramuscular dose* is 25 mg. (1 cc.). If necessary, and if no hypotension occurs, repeat the initial dose in one hour. Subsequent dosages should be oral, starting at 25 mg. to 50 mg. t.i.d.

Somatic Conditions Complicated by Emotional Stress–*Starting oral dosage* is 10 mg. to 25 mg. t.i.d. or q.i.d. Increase gradually by 10 mg. to 25 mg. increments at semiweekly or weekly intervals. *Starting intramuscular dosage* is 25 mg. (1 cc.), repeated after one hour if necessary and if no hypotension occurs.

Hospitalized Psychiatric Patients – ***Acutely agitated, manic, or disturbed patients:*** *Starting intramuscular dose* is 25 mg. (1 cc.). If no marked hypotension occurs, an additional 25 mg. to 50 mg. injection may be given after one hour. Subsequent intramuscular dosages may be increased gradually over a period of several days – even up to 400 mg. q4-6h in exceptionally severe cases – until the patient is controlled. (In elderly or emaciated patients the dosage should be increased more slowly than in other patients.) Usually the patient becomes quiet and cooperative within 24 to 48 hours after the initial dose, at which time oral doses may gradually be substituted for intramuscular doses (mg. for mg. or higher). Even if control is not complete, oral doses may gradually replace intramuscular doses. During this period, oral dosage should be increased rapidly until the patient is calm. Usually an *oral dose* of 500 mg. a day is sufficient but, if necessary, the dosage may be gradually increased still further to 2,000 mg. a day or higher. ***Less acutely agitated patients:*** *Starting oral dose* is 25 mg. t.i.d. Subsequently, increase the amount gradually until an effective dosage is reached – usually 400 mg. daily is sufficient. ***Duration of therapy:*** It is important to determine the optimal dosage regimen and to continue treatment long enough for maximum clinical response. Maximum improvement is sometimes not apparent until after weeks or even months of therapy.

Nausea and Vomiting – *Starting oral dosage* is 10 mg. to 25 mg. q4-6h, p.r.n., and may be increased if necessary. *Starting intramuscular dose* is 25 mg. (1 cc.). If no hypotension occurs subsequent doses of 25 mg. to 50 mg. q3-4h, p.r.n., may be given until vomiting is checked. Then replace intramuscular administration with oral. *Starting rectal dosage* is one 100 mg. suppository q6-8h, p.r.n. In some patients, one-half this dose may be sufficient.

Hiccups – *Starting oral dosage* is 25 mg. to 50 mg. t.i.d. or q.i.d. If after 2-3 days symptoms persist, *an intramuscular dosage* of 25 mg. to 50 mg. (1-2 cc.) may be used. *Use intravenous administration* only when symptoms still persist. By slow infusion, 25 mg. to 50 mg. (1-2 cc.) should be administered in 500 cc. to 1,000 cc. of physiologic saline solution, with the patient kept flat in bed. Follow blood pressure closely.

Alcoholism – ***Severely agitated patients:*** *Starting intramuscular dose* is 25 mg. to 50 mg. (1-2 cc.). Repeat initial dose if necessary and if no hypotension occurs. Start subsequent oral dosages at 25 mg. to 50 mg. t.i.d. ***Agitated but manageable patients:*** *Starting oral dose* is 50 mg., followed by 25 mg. to 50 mg. t.i.d. ***Ambulatory patients with withdrawal symptoms or sober chronic alcoholics:*** *Starting oral dose* is 10 mg. t.i.d. or q.i.d., or 25 mg. b.i.d. or t.i.d. Patients in a stuporous condition should be allowed to sleep off some of the effects of the alcohol before 'Thorazine' is administered.

Cancer and Pain – ***Severe pain:*** *starting intramuscular dosage* is 25 mg. (1 cc.) b.i.d. or t.i.d. ***Milder pain:*** starting oral *dosage* is 10 mg. t.i.d. or q.i.d., or 25 mg. b.i.d. or t.i.d. Because 'Thorazine' potentiates their action, reduce the dosage of narcotics or sedatives to ¼ to ½ of the pre-'Thorazine' level.

Obstetrics – *Intramuscular dose* in labor and delivery is 12.5 mg. to 25 mg. (0.5-1 cc.), administered when dilation of the cervix reaches 3 to 5 centimeters or when strong labor is established. At the same time (but not mixed in the syringe with 'Thorazine'), ¼ to ½ the usual dose of a narcotic or sedative and, if desired, 0.4 mg. of scopolamine may be administered. Depending upon blood pressure, respiration and the general condition of the patient, the initial 'Thorazine' dose (alone or with reduced amounts of the other agents) may be repeated in 3 to 5 hours if necessary.

Surgery (Adults) – ***Preoperatively,*** *oral dose* is 25 mg. to 50 mg., 2 to 3 hours before the operation. *Intramuscular dose* is 12.5 mg. to 25 mg. (0.5-1 cc.), 1 to 2 hours before the operation. ***During surgery*** 'Thorazine' should be administered only if needed to control nausea and vomiting, retching, hiccups, or other acute symptoms. *Intramuscular dose* is 12.5 mg. (0.5 cc.), repeated in ½ hour if necessary and if no hypotension occurs.

Intravenous dose should be no more than 2 mg. per fractional injection, with injections at not less than 2-minute intervals. Also, it should not exceed 25 mg. 'Thorazine' should be diluted to 1 mg./cc. (1 cc. mixed with 24 cc. of physiologic saline solution). ***Postoperatively,*** *oral dosage* is 10 mg. to 25 mg. q4-6h, p.r.n. *Intramuscular dosage* is 12.5 mg. to 25 mg. (0.5-1 cc.), repeated in one hour if necessary and if no hypotension occurs.

PEDIATRIC DOSAGE AND ADMINISTRATION

Nausea and Vomiting, Behavior Disorders and Pain – *Oral dosage* is on the basis of ¼ mg./lb. of body weight q4-6h, until symptoms are controlled (i.e., for 40 lb. child—10 mg. q4-6h). Calculate 'Thorazine' Syrup dosage at 10 mg./5 cc. tsp. *Rectal dosage* is on the basis of ½ mg./lb. of body weight q6-8h, p.r.n. (i.e., for 20-30 lb. child—half of a 25 mg. suppository q6-8h). *Intramuscular dosage* is on the basis of ¼ mg./lb. of body weight q6-8h, p.r.n. In children up to 5 years (or 50 lbs.)—not over 40 mg./day. In children 5-12 years (or 50-100 lbs.)—not over 75 mg./day.

Pain—Because 'Thorazine' potentiates the action of narcotics and sedatives, reduce the dosage of these agents to ¼ to ½ of the pre-'Thorazine' level.

Behavior Disorders—In severe cases, 50-100 mg. daily has been used and, in older children, 200 mg. or more daily may be required.

Surgery (Children) – ***Preoperatively,*** dose is on the basis of ¼ mg./lb. of body weight given either orally 2 to 3 hours before the operation, or intramuscularly 1 to 2 hours before. ***During surgery,*** the dose is on the basis of ⅛ mg./lb. of body weight, repeated in ½ hour if necessary and if no hypotension occurs. The intravenous dose should be no more than 1 mg. per fractional injection, with injections at not less than 2-minute intervals. Intravenous dosage during surgery should not exceed recommended intramuscular dosage and should always be diluted to 1 mg./cc. ***Postoperatively,*** dosage is on the basis of ¼ mg./lb. of body weight, either orally q4-6h, p.r.n., or intramuscularly, a single dose repeated in one hour if necessary and if no hypotension occurs.

NOTES ON PARENTERAL ADMINISTRATION

Except for acute ambulatory cases, parenteral administration should generally be reserved for bedfast patients. Parenteral administration should always be made with the patient lying down and remaining so for at least ½ hour afterward because of possible hypotensive effects. The injection should be given *slowly, deep* into the upper outer quadrant of the buttock. If irritation and pain at the site of injection are problems, dilution of 'Thorazine' Injection with physiologic saline solution or 2% procaine solution may be helpful. Subcutaneous administration is not advisable, and care should be taken to avoid injecting undiluted 'Thorazine' Injection into a vein. Intravenous administration is recommended only for severe hiccups and surgery.

Because contact dermatitis has been reported, avoid getting the solution on hands or clothing.

SIDE EFFECTS

The drowsiness caused by 'Thorazine' may be unwanted in some patients. It is usually mild to moderate and disappears after the first or second week of therapy. If, however, drowsiness is troublesome, it can usually be controlled by lowering the dosage or by administering small amounts of dextro amphetamine.

Other side effects that have been reported occasionally are dryness of the mouth, nasal congestion, some constipation, miosis in a few patients and, very rarely, mydriasis. Mild fever (99°F.) may occur occasionally during the first days of therapy with large intramuscular doses. During 'Thorazine' therapy some patients have an increased appetite and gain weight. Usually these patients reach a plateau beyond which they do not gain further weight.

CAUTIONS

Jaundice: In the more than 14 million patients who have been treated with 'Thorazine' in the United States, the incidence of jaundice—regardless of indication, dosage, or mode of administration—has been low. Few cases have occurred in less than one week or after six weeks. Jaundice due to 'Thorazine' is of the so-called "obstructive" type; is without parenchymal damage; and is usually promptly reversible upon the withdrawal of 'Thorazine'. Because detailed liver function tests of 'Thorazine'-induced jaundice give a picture which mimics extrahepatic obstruction, exploratory laparotomy should be withheld until sufficient studies confirm extrahepatic obstruction.

Agranulocytosis: Agranulocytosis, although rare, has been reported in patients on 'Thorazine' therapy. Patients receiving 'Thorazine' should be observed regularly and asked to report at once the sudden appearance of sore throat or other signs of infection. If white blood counts and differential smears give an indication of cellular depression, the drug should be discontinued, and antibiotic and other suitable therapy should be instituted. Because most reported cases have occurred between the fourth and the tenth weeks of treatment, patients on prolonged therapy should be observed particularly during that period.

A moderate suppression of total white blood cells is sometimes observed in patients on 'Thorazine' therapy. If not accompanied by other symptoms, it is not an indication for discontinuing 'Thorazine'.

Potentiation: 'Thorazine' prolongs and intensifies the action of many central nervous system depressants, such as barbiturates and narcotics. Consequently, it is advisable to stop administration of such depressants before initiating 'Thorazine' therapy. Later the depressant agents may be reinstated, starting with low doses, and increasing according to response. Approximately ¼ to ½ the usual dosage of such agents is required when they are given in combination with 'Thorazine'. (However, 'Thorazine' does not potentiate the anticonvulsant action of barbiturates. In patients who are receiving anticonvulsants, the dosage of these agents—including barbiturates—should not be reduced if 'Thorazine' is started. Rather, 'Thorazine' should be started at a very low dosage and increased, if necessary.)

Hypotensive Effect: Postural hypotension and simple tachycardia may be noted in some patients. In these patients, momentary fainting and some dizziness are characteristic and usually occur shortly after the first parenteral dose, occasionally after a subsequent parenteral dose—very rarely after the first oral dose. In most cases, prompt recovery is spontaneous and all symptoms disappear within ½ to 2 hours with no subsequent ill effects. Occasionally, however, this hypotensive effect may be more severe and prolonged, producing a shock-like condition. In consideration of possible hypotensive effects, the patient should be kept under observation (preferably lying down) for some time after the initial parenteral dose. If, on rare occasions, hypotension does occur, it can ordinarily be controlled by placing the patient in a recumbent position with head lowered and legs raised. If it is desirable to administer a vasoconstrictor, 'Levophed' and 'Neo-Synephrine'★ are the most suitable. Other pressor agents, including epinephrine, are not recommended because phenothiazine derivatives may reverse the usual elevating action of these agents and cause a further lowering of blood pressure.

Antiemetic Effect: The physician should always bear in mind that the antiemetic effect of 'Thorazine' may mask signs of overdosage of toxic drugs and may obscure diagnosis of conditions such as intestinal obstruction and brain tumor.

Dermatological Reactions: Dermatological reactions have been reported. Most have been of a mild urticarial type, suggesting allergic origin. Some of them appear to be due to photosensitivity, and it is advisable that patients on 'Thorazine' avoid undue exposure to the summer sun.

Neuromuscular Reactions: With very large doses of 'Thorazine', as frequently used in psychiatric cases over long periods, there have been a few patients who have exhibited neuromuscu-

★'Levophed' and 'Neo-Synephrine' are the trademarks (Reg. U.S. Pat. Off.) of Winthrop Laboratories for its brands of levarterenol and phenylephrine respectively.

lar reactions (extrapyramidal symptoms) which closely resemble parkinsonism. Such symptoms are reversible and usually disappear within a short time after the dosage has been decreased or the drug withdrawn. These neuromuscular reactions can also be controlled by the concomitant administration of standard anti-parkinsonism agents.

Lactation: Moderate engorgement of the breast with lactation has been observed in female patients receiving very large doses of 'Thorazine'. This, however, is a transitory condition which disappears on reduction of dosage or withdrawal of the drug.

CONTRAINDICATIONS

In comatose states due to central nervous system depressants (alcohol, barbiturates, narcotics, etc.), and also in patients under the influence of large amounts of barbiturates or narcotics.

AVAILABLE

Tablets, 10 mg., 25 mg., 50 mg. and 100 mg., in bottles of 50, 500 and 5000; 200 mg., for use in mental hospitals, in bottles of 500 and 5000. (Each tablet contains chlorpromazine hydrochloride, 10 mg., 25 mg., 50 mg., 100 mg., or 200 mg.)

Ampuls, 1 cc. and 2 cc. (25 mg./cc.), in boxes of 6, 100 and 500. (Each cc. contains, in aqueous solution, chlorpromazine hydrochloride, 25 mg.; ascorbic acid, 2 mg.; sodium bisulfite, 1 mg.; sodium sulfite, 1 mg.; sodium chloride, 6 mg.)

Multiple-dose Vials, 10 cc. (25 mg./cc.), in boxes of 1, 20 and 100. (Each cc. contains, in aqueous solution, chlorpromazine hydrochloride, 25 mg.; ascorbic acid, 2 mg.; sodium bisulfite, 1 mg.; sodium sulfite, 1 mg.; sodium chloride, 1 mg. Contains benzyl alcohol, 2%, as preservative).

Spansule® capsules, 30 mg., 75 mg., 150 mg. and 200 mg., in bottles of 30, 250 and 1500; also 300 mg., in bottles of 30 and 1500. (Each 'Spansule' capsule contains chlorpromazine hydrochloride, 30 mg., 75 mg., 150 mg., 200 mg., or 300 mg.)

Syrup, 10 mg./teaspoonful (5 cc.), in 4 fl. oz. bottles. (Each 5 cc. contains chlorpromazine hydrochloride, 10 mg.)

Suppositories, 25 mg. and 100 mg., in boxes of 6. (Each suppository contains chlorpromazine, 25 mg. or 100 mg.; glycerin, glyceryl monopalmitate, glyceryl monostereate, hydrogenated cocoanut oil fatty acids, hydrogenated palm kernel oil fatty acids, lecithin.)

Concentrate (for hospital use), 30 mg./cc., in 4 fl. oz. bottles, packages of 12 and 36; and in 1 gal. bottles. (Each cc. contains chlorpromazine hydrochloride, 30 mg.)

Prescribing information adopted January, 1961

COMPAZINE®

brand of prochlorperazine

PRESCRIBING INFORMATION

Antiemetic • Tranquilizer

'Compazine' provides a beneficial calming effect and prompt antiemetic action with unusual freedom from drowsiness and depressing effect. Clinical experience in several million patients has shown 'Compazine' to be promptly effective in low dosage, with minimal side effects in the dosage range recommended for everyday practice.

INDICATIONS

*1. **Anxiety, tension, agitation,*** confusion, chronic alcoholism and behavior disorders in children.

*2. **Emotional stress associated with somatic conditions*** such as g.i. disorders, cardiovascular conditions, hypertension, menopause, premenstrual tension, neurodermatitis, arthritis, asthma, cancer, tuberculosis and tension headache.

*3. **Nausea and vomiting of widely varying causes*** such as pregnancy, postoperative conditions, viral gastroenteritis and other infectious conditions, irradiation therapy and motion sickness. In most patients, relief is provided within a short time after one oral dose.

*4. **In surgery and obstetrics*** to prevent or control: (a) nausea, vomiting and retching; and (b) fear, tension and restlessness.

*5. **In psychiatry*** to control agitation, anxiety, tension and confusion that may be seen in psychotic states.

ADMINISTRATION AND USUAL DOSAGE

Dosage should be determined according to the severity of the condition and the response of the patient. It is important to begin therapy with the lowest recommended dosage. In hospitalized patients or those under adequate supervision, higher doses may be indicated.

USUAL ADULT DOSAGE

Tablets: The usual starting dosage is 5 mg. three or four times daily. Some patients will respond better when subsequent dosage is raised to 10 mg. t.i.d. or q.i.d. Dosage over 40 mg. daily should be used only in resistant cases.

Spansule® sustained release capsules: The usual starting dosage is one 15 mg. 'Spansule' capsule taken upon arising, or one 10 mg. 'Spansule' capsule in the morning and evening. Some patients may subsequently require dosage increased to one 30 mg. capsule in the morning. Dosage over 40 mg. daily should be used only in resistant cases. (B.i.d. dosage of the 30 mg. capsule should be limited to severe cases.)

Dosage recommendations for other oral forms of 'Compazine' may be applied to 'Compazine' *Spansule* capsules on the basis of the total daily dose in milligrams. (For example: one 15 mg. 'Compazine' *Spansule* capsule replaces 5 mg. 'Compazine' Tablets, t.i.d.) All strengths have the same *duration* of action. They differ only in *intensity* of therapeutic effect.

In "morning sickness" of pregnancy, one 'Compazine' *Spansule* capsule taken before retiring affords antiemetic activity throughout the night and into the morning, thus protecting against "morning sickness."

The 15 mg. 'Compazine' *Spansule* capsule is ideal for once-a-day administration. The 10 mg. 'Compazine' *Spansule* capsule is ideal for twice-a-day (q12h) administration.

Syrup: 5 mg. to 10 mg. (1 to 2 teaspoonfuls) three or four times daily.

Suppositories: Usual dosage in adults is one 25 mg. 'Compazine' Suppository twice daily.

Injection: Total parenteral dosage in 24 hours should not exceed 40 mg.

For intramuscular administration, an initial dose of 5 mg. to 10 mg. (1 to 2 cc.) of 'Compazine' Injection should be injected *deeply* into the upper outer quadrant of the buttock. Repeat, if necessary, at intervals of 3 to 4 hours. Pain at the site of injection has not been a problem. ***For intravenous administration,*** see surgery section. Dilution is not required. ***Subcutaneous administration*** is not advisable because of local irritation.

It is recommended that 'Compazine' Injection not be mixed with other agents in the syringe.

Dermatitis due to contact with 'Compazine' has not been a problem. However, it is recommended that nurses or others giving frequent injections take precautions to avoid getting the solution on their hands or clothing.

'Compazine' Injection should be protected from light, since exposure may cause discoloration. Slight yellowish discoloration will not significantly alter the potency or therapeutic efficacy. However, if markedly discolored, the solution should be discarded.

IN SURGERY (Adults)

ROUTE	DOSAGE
preoperatively	
Intramuscular injection	5 mg. to 10 mg. (1-2 cc.)

1 to 2 hours before induction of anesthesia. Repeat once in 30 minutes if necessary.

ROUTE	DOSAGE
Intravenous injection	5 mg. to 10 mg. (1-2 cc.)

15 to 30 minutes before induction of anesthesia.

Intravenous infusion	20 mg. (4 cc.) per liter of isotonic solution

Add to I.V. infusion 15 to 30 minutes before induction. Repeat once if necessary.

during surgery	
Intramuscular or Intravenous injection	5 mg. to 10 mg. (1-2 cc.)

When needed to control acute symptoms. Repeat once if necessary.

postoperatively

To prevent anxiety, nausea, vomiting, or emergence excitement, add to I.V. infusion: 20 mg. (4 cc.) per liter of isotonic solution.

For immediate control of acute nausea, vomiting, retching, or emergence excitement, inject 5 mg. to 10 mg. (1-2 cc.), I.V. or I.M. Repeat once if necessary.

IN OBSTETRICS

'Compazine' dosage should be adjusted to the individual patient and her condition in accordance with the general use of the drug (i.e., 5 mg. to 10 mg. per dose; 15 mg. to 40 mg. per day). The following dosage suggestions should prove satisfactory for the majority of obstetric patients.

To relieve anxiety or prevent vomiting during the first stage of labor, the usual dosage is 10 mg. of 'Compazine' by intramuscular injection. As labor progresses, or if it is prolonged, subsequent 10 mg. doses may be administered as needed. The total daily dose need rarely exceed 30 mg.

To control postpartum anxiety or nausea and vomiting, the usual total daily dose of 'Compazine' is 15 mg. to 30 mg. administered orally or intramuscularly.

NOTE: 'Compazine' has no clinically significant potentiating effect on narcotics, anesthetics, or sedatives. However, because the 'Compazine' patient is calm and relaxed, it is sometimes possible to produce satisfactory analgesia with less than the customary amounts of these agents. This lack of potentiating effect also minimizes the risk of intensifying or prolonging the effect of residual anesthetics and other depressant agents used in surgery or labor and delivery.

As with intravenous administration of any surgical or obstetric adjuvant, the increased possibility of hypotension should be kept in mind if 'Compazine' is administered by either intravenous injection or infusion.

USUAL CHILDREN'S DOSAGE

It is important always to use the lowest effective dosage, because as dosage is raised the possibility of side effects increases. There have been occasional cases of neuromuscular reactions (extrapyramidal symptoms) in children. These have been transitory and reversible.

Nausea and vomiting are usually controlled during the first day of therapy. Therefore more than one day's therapy is seldom necessary.

Weight	Dosage	Not to exceed
Under 20 lbs.	not recommended	
20-29 lbs.	2.5 mg. once or twice a day	7.5 mg. per day
30-39 lbs.	2.5 mg. b.i.d. or t.i.d.	10.0 mg. per day
40-85 lbs.	2.5 mg. t.i.d. or 5 mg. b.i.d.	15.0 mg. per day

For behavior disorders, dosage may be increased gradually, if necessary, within the following daily limits:

2 to 6 years of age: Total daily dose should not exceed 20 mg.
6 to 12 years of age: Total daily dose should not exceed 25 mg.

For rapid control of nausea and vomiting or behavior disorders:

Injection: For children under 12 years of age, each dose should be calculated on the basis of 0.06 mg. of 'Compazine' per pound of body weight and should be administered by deep intramuscular injection. For example, a 40-pound child would receive an injection of 2.5 mg. (0.5 cc.). Control is usually obtained with a single dose.

'COMPAZINE' IN PSYCHIATRY

'Compazine' is indicated for control of agitation, anxiety, tension and confusion that may be seen in such conditions as schizophrenias; manic-depressive states, manic phase; severe personality disorders; involutional psychoses; degenerative conditions; and senile psychoses.

ADULTS

Oral psychiatric dosage: ***In relatively mild conditions,*** as may be seen in private psychiatric practice or on outpatient clinics, the suggested starting dosage is 5 mg. t.i.d. or q.i.d. Some patients will respond better when subsequent dosage is raised to 10 mg. t.i.d. or q.i.d. ***In moderate or severe conditions,*** when patients are either hospitalized or under adequate supervision, the suggested starting dosage is 10 mg. t.i.d. or q.i.d. Dosage should be increased gradually until symptoms are controlled or side effects become bothersome. Experience has shown that when dosage is increased gradually (by small increments every two or three days) side effects either do not occur or are easily controlled.

Some patients will obtain satisfactory results on 50 mg. to 75 mg. of 'Compazine' daily. In more severe disturbances, the optimum dosage in most patients is 100 mg. to 150 mg. daily. With oral administration, response ordinarily becomes evident within a day or two. Longer periods of treatment are usually required before maximal improvement is obtained.

I.M. psychiatric dosage: For immediate control of severely disturbed adult patients, an initial dose of 10 mg. to 20 mg. (2-4 cc.) should be injected deeply into the upper outer quadrant of the buttock. If necessary, this dose should be repeated every 2 to 4 hours to gain control of the patient. Patients often respond shortly after the first injection. In resistant cases, the initial dose may be repeated hourly. More than three or four doses are seldom necessary. If, in rare cases, parenteral medication is indicated over a prolonged period, 10 mg. to 20 mg. (2-4 cc.) at 4- to 6-hour intervals is the usual dosage. Pain and irritation at the site of injection have rarely been encountered and some patients have been given the drug intramuscularly for periods of several weeks. After control is achieved by intramuscular administration, most patients can be switched to an oral form of the drug at the same dosage level or higher.

CHILDREN *(2 to 12 years)*

Oral psychiatric dosage: The suggested children's starting dosage in psychiatry is 2.5 mg. (½ teaspoonful of syrup) two or three times daily, or 5 mg. (one teaspoonful of syrup or one 5 mg. tablet) twice daily, according to body weight. During the first day, the total daily dose should not exceed 10 mg. Dosage is then increased according to the patient's response. (2.5 mg. and 5 mg. suppositories are also available.)

For ages 2 to 6, the total daily dosage usually does not exceed 20 mg. ***For ages 6 to 12,*** the total daily dosage usually does not exceed 25 mg. Because extrapyramidal symptoms have been reported in children as well as in adults, it is important to use the lowest effective dosage.

SIDE EFFECTS

In the dosage range recommended for everyday practice, side effects have been infrequent, transitory and usually mild. A few patients may experience a mild drowsiness when first taking 'Compazine'. There may also be occasional cases of dizziness,

skin reaction and neuromuscular reactions (extrapyramidal symptoms); rarely, hypotension.

Neuromuscular Reactions

Occasionally, neuromuscular reactions (extrapyramidal symptoms) have been observed with 'Compazine' therapy. It is important, therefore, to use the lowest effective dosage, because as dosage is raised the possibility of these reactions increases.

Motor Restlessness: A few patients on 'Compazine'—particularly those in whom dosage has been raised to higher levels—may experience a transient unpleasant stimulation or jitteriness, characterized by restlessness and insomnia. The dosage of 'Compazine' should not be increased while these side effects are present. Patients should be reassured that such effects are temporary and will disappear spontaneously. In those cases where the symptoms are particularly bothersome, reduction of dosage or the concomitant administration of a sedative may be helpful.

Dystonias: These neuromuscular reactions are seen in a significant percentage of hospitalized mental patients on high dosages. The muscles of the face and shoulder girdle may be selectively involved. Symptoms observed have included spasm of the neck muscles, extensor rigidity of back muscles, carpopedal spasm, eyes rolled back, trismus and swallowing difficulty. Despite some similarity to symptoms of serious neurologic disorders, these reactions are usually promptly reversible by temporary discontinuance of 'Compazine' therapy and administration of a sedative such as phenobarbital. The dosage and route of administration should be determined according to the severity of the symptoms. Patients should be reassured that the symptoms are transitory. Depending on the severity of the dystonia, suitable supportive measures, such as maintaining a clear airway and adequate hydration, should be employed. Note: It has been reported that injectable administration of Benadryl* may also be helpful.

Pseudo-parkinsonism: These neuromuscular reactions may resemble the classic parkinsonism syndrome. Treatment should include temporary discontinuance of 'Compazine' therapy and the administration of any standard anti-parkinsonism agent (see *PDR*). Patients should also be reassured that these symptoms are transitory. Depending on the severity of symptoms, suitable supportive measures, such as maintaining a clear airway and adequate hydration, should be employed.

CAUTIONS

Clinical experience has demonstrated that 'Compazine', a phenothiazine derivative, has a wide margin of safety and that there is little likelihood of blood or liver toxicity. The physician should be aware, however, of their possible occurrence.

The antiemetic action of 'Compazine' may mask signs of overdosage of toxic drugs or may obscure the diagnosis of conditions such as intestinal obstruction and brain tumor.

'Compazine' has no clinically significant potentiating action. However, if depressant agents are used in conjunction with this drug, the possibility of an additive effect should be kept in mind.

CONTRAINDICATIONS

'Compazine' is contraindicated in comatose or greatly depressed states due to central nervous system depressants.

AVAILABLE

There is a dosage form of 'Compazine' for every medical need. **Tablets,** 5 mg. and 10 mg. and, for use in psychiatry, 25 mg., in bottles of 50, 500 and 5000. Each tablet contains 5 mg., 10 mg., or 25 mg. of prochlorperazine as the dimaleate.

'Spansule' capsules, 10 mg., 15 mg. and 30 mg., in bottles of 30, 250 and 1500; and, for use in psychiatry, 75 mg., in bottles of 30 and 1500. Each capsule contains 10 mg., 15 mg., 30 mg., or 75 mg. of prochlorperazine as the dimaleate.

Ampuls, 2 cc. (5 mg./cc.), in boxes of 6, 100 and 500. Each cc. contains, in aqueous solution: 5 mg. prochlorperazine as the ethanedisulfonate, 1 mg. sodium sulfite, 1 mg. sodium bisulfite, 8 mg. sodium phosphate and 12 mg. sodium biphosphate.

Multiple-dose Vials, 10 cc. (5 mg./cc.), in boxes of 1, 20 and 100. Each cc. contains, in aqueous solution: 5 mg. prochlorperazine as the ethanedisulfonate, 5 mg. sodium biphosphate, 12 mg. sodium tartrate, 0.9 mg. of sodium saccharin and 0.75% benzyl alcohol as preservative.

Suppositories, 2½ mg. (for young children), 5 mg. (for older children) and 25 mg. (for adults), in boxes of 6. Each suppository contains: 2½ mg., 5 mg., or 25 mg. of prochlorperazine with glycerin, glyceryl monopalmitate, glyceryl monostearate, hydrogenated cocoanut oil fatty acids, hydrogenated palm kernel oil fatty acids and lecithin.

Syrup, 5 mg./teaspoonful (5 cc.), in 4 fl. oz. bottles. Each 5 cc. contains 5 mg. of prochlorperazine as the ethanedisulfonate.

Concentrate (for hospital use), 10 mg./cc. in 4 fl. oz. bottles, cartons of 12 and 36. Each cc. contains 10 mg. of prochlorperazine as the ethanedisulfonate.

Prescribing information also available in *Compazine® Reference Manual, Physicians' Desk Reference,* or from your SK&F representative or your pharmacist.

Prescribing information adopted January 1961.

STELAZINE®

brand of trifluoperazine

PRESCRIBING INFORMATION

INDICATIONS

In general practice and in psychiatry 'Stelazine' is outstanding among tranquilizers because it relieves anxiety, agitation and tension—without sedation. Nor does it cause euphoria. 'Stelazine' is also effective in relieving anxiety either accompanying or causing somatic conditions. Where anorexia and insomnia are problems, 'Stelazine' usually produces a marked improvement in appetite and sleep patterns.

'Stelazine' provides a fast therapeutic response. On a convenient b.i.d. dosage regimen, many patients who have failed to respond to other agents, or have responded only poorly, are promptly relieved of their symptoms. With symptoms allayed, rapport with the physician is facilitated, and patients are more receptive to counselling or psychotherapy.

In hospitalized psychiatric patients 'Stelazine' produces rapid response in many diagnostic categories. These include acute and chronic schizophrenias, manic-depressive psychoses, involutional psychoses, chronic brain syndrome and mental deficiency.

'Stelazine' can combat psychotic symptoms without causing drowsiness. It can quiet hyperactive patients and activate withdrawn patients, and it has a marked beneficial effect on delusions and hallucinations.

'Stelazine' can rapidly terminate acute psychotic episodes. On the admissions service, intensive 'Stelazine' therapy often results in early discharges.

Also noteworthy is the effectiveness of 'Stelazine' in the treatment of hard-core, chronic and refractory schizophrenics. When administered to a group of such patients, it characteristically produces significant improvement in at least 30% to 40% of them.

ADMINISTRATION AND DOSAGE

Dosage of 'Stelazine' should be adjusted to the needs of the individual.

*Trademark Reg. U.S. Pat. Off.: 'Benadryl' for diphenhydramine hydrochloride, Parke-Davis.

1. Adult Dosage for Use in Everyday Practice
The recommended dosage is 1 mg. or 2 mg. twice daily. In everyday practice, optimal results are usually achieved within this range, so that it is seldom necessary to exceed 4 mg. daily.

Because of the inherent long action of 'Stelazine', patients may be controlled on convenient b.i.d. administration; some patients may be maintained on once-a-day administration.

2. Adult Dosage for Use in Psychiatric Practice
oral (for office patients and outpatients with anxiety): The usual starting dosage is 1 mg. or 2 mg. b.i.d. In the treatment of these patients, it is seldom necessary to exceed 4 mg. a day. (Some patients with more severe disturbances, and discharged mental patients, may require higher dosages.) In some patients, maintenance dosage can be reduced to once-a-day administration.

oral (for patients who are either hospitalized or under adequate supervision): The usual starting dosage is 2 mg. to 5 mg. b.i.d. (Small or emaciated patients should always be started on the lower dosage.)

The majority of patients will show optimum response on 15 mg. or 20 mg. daily, although a few may require 40 mg. a day or more. It is important to give doses that are high enough for long enough periods of time – especially in chronic patients.

Optimum therapeutic dosage levels should be reached within two or three weeks after the start of therapy. When maximum therapeutic response is achieved, dosage may be reduced gradually to a satisfactory maintenance level.

intramuscular (for prompt control of severe symptoms): The usual dosage is 1 mg. to 2 mg. (½-1 cc.) by deep intramuscular injection q4-6h, p.r.n. More than 6 mg. within 24 hours is rarely necessary. As soon as a satisfactory response is observed, oral medication should be substituted at the same dosage level or slightly higher.

Only in very exceptional cases should intramuscular dosage exceed 10 mg. within 24 hours. Since 'Stelazine' has a relatively long duration of action, injections should not be given at intervals of less than 4 hours because of the possibility of an excessive cumulative effect.

'Stelazine' Injection has been exceptionally well tolerated; there is little, if any, pain and irritation at the site of injection.

3. Dosage for Psychotic and Mentally Defective Children
The dosages given below apply to children, ages 6 to 12, who are either hospitalized or under adequate supervision.

oral: The starting dosage is 1 mg. administered once a day or b.i.d., depending on the size of the child. Dosage may be increased gradually until symptoms are controlled or until side effects become troublesome. Both the rate and the amount of dosage increases should be carefully adjusted to the size of the child and the severity of the symptoms, and the lowest effective dosage should always be used. Once control is achieved, it is usually possible to reduce dosage to a satisfactory maintenance level.

In most cases, it is not necessary to exceed 15 mg. of 'Stelazine' daily. However, some older children with severe symptoms may require, and be able to tolerate, higher dosages.

intramuscular: There has been little experience with the use of 'Stelazine' Injection in children. However, if it is necessary to achieve rapid control of severe symptoms, 1 mg. (½ cc.) of 'Stelazine' may be administered intramuscularly once or twice a day, depending on the size of the child. Once control is achieved, usually after the first day, the oral dosage forms of 'Stelazine' should be substituted for the Injection.

SIDE EFFECTS

In the dosage range of 2-4 mg. daily, side effects from 'Stelazine' are infrequent. When they do occur, they are usually slight and transitory. Mild drowsiness occurs in a small percentage of patients; this usually disappears after a day or two of 'Stelazine' therapy. There are occasional cases of dizziness, mild skin reaction, dry mouth, insomnia and fatigue; rarely, neuromuscular (extrapyramidal) reactions.

In hospitalized psychiatric patients receiving daily 'Stelazine' dosages of 10 mg. or more, clinical experience has shown that, when side effects occur, their appearance is usually restricted to the first two or three weeks of therapy. After this initial period, they appear infrequently, even in the course of prolonged therapy. Termination of 'Stelazine' therapy because of side effects is rarely necessary.

Side effects observed include dizziness, muscular weakness, extrapyramidal symptoms, anorexia, rash, lactation and blurred vision. Drowsiness has occurred, but has been transient, usually disappearing in a day or two.

Neuromuscular (Extrapyramidal) Reactions
These symptoms are seen in a significant number of hospitalized mental patients receiving 'Stelazine'. They may be characterized by motor restlessness, be of the dystonic type, or they may resemble parkinsonism.

motor restlessness: Some patients may experience an initial transient period of stimulation or jitteriness, chiefly characterized by motor restlessness and sometimes insomnia. These patients should be reassured that this effect is temporary and will disappear spontaneously. The dosage of 'Stelazine' should not be increased while these side effects are present.

If this turbulent phase becomes too troublesome, the symptoms can be controlled by a reduction of dosage or the concomitant administration of a barbiturate.

dystonias: These symptoms are rare outside of mental hospitals, but they may be observed occasionally in patients who have received 'Stelazine' as a mild tranquilizer.

Symptoms may include: spasm of the neck muscles, sometimes progressing to torticollis; extensor rigidity of back muscles, sometimes progressing to opisthotonos; carpopedal spasm, trismus, swallowing difficulty, oculogyric crisis and protrusion of the tongue.

The onset of the dystonias may be sudden. A primary characteristic of these symptoms is their intermittency. They may last several minutes, disappear and then recur. There is typically no loss of consciousness and definite prodromata are usually present. Initially, these intermittent symptoms occur in a crescendo of intensity. Then as the effect of the drug wears off, the intervals between the occurrence of symptoms become longer, and the intensity of the symptoms subsides.

Despite their similarity to symptoms of serious neurological disorders, these dystonias are usually promptly reversible and need not cause undue alarm. They usually subside gradually within a few hours, and almost always within 24 to 48 hours, after the drug has been temporarily discontinued. If 'Stelazine' therapy is discontinued, it should be reinstituted at a lower dosage.

Treatment is symptomatic and conservative. *In mild cases,* reassurance of the patient is often sufficient therapy. Barbiturates are also useful. *In moderate cases,* barbiturates will usually bring rapid relief. The dosage and route of administration of the barbiturate used should be determined by the intensity of the symptoms and the response of the patient. *In more severe adult cases,* the administration of an anti-parkinsonism agent (see *Physicians' Desk Reference)* produces rapid, often dramatic, reversal of symptoms. Also, intravenous caffeine and sodium benzoate seems to be an effective and rapid antagonist to the dystonias. Depending on the severity of the dystonia, suitable supportive measures such as maintaining a clear airway and adequate hydration should be employed. *In children,* reassurance and barbiturates will usually control symptoms. Dosage and route of administration should be determined according to the intensity of symptoms and response of patient.

Note: It has been reported that injectable administration of 'Benadryl' may also be helpful in controlling dystonias.

pseudo-parkinsonism: These symptoms are extremely rare outside of mental hospitals.

Symptoms include: mask-like facies; drooling; tremors; pill-rolling motion; and shuffling gait.

Reassurance and sedation are important components of effective therapy. In the majority of cases these symptoms are readily reversible when an anti-parkinsonism agent is administered concomitantly with 'Stelazine'. Occasionally it is necessary to lower the dosage or to temporarily discontinue the drug. Depending on the severity of symptoms, suitable supportive measures such as maintaining a clear airway and adequate hydration should be employed. If 'Stelazine' therapy is discontinued, it should be reinstituted at a lower dosage.

CAUTIONS

Clinical experience has demonstrated that 'Stelazine', a phenothiazine derivative, has a wide range of safety and that there is little likelihood of either blood or liver toxicity. The physician should be aware, however, of their possible occurrence.

One of the results of 'Stelazine' therapy may be an increase in mental and physical activity. In some patients, this effect may not be desired. For example, although 'Stelazine' has relieved anxiety and, at the same time, anginal pain in patients with angina pectoris, a few such patients have complained of increased pain while taking 'Stelazine'. Therefore, if 'Stelazine' is used in angina patients, they should be observed carefully and, if an unfavorable response is noted, the drug should be withdrawn.

Hypotension has not been a problem, but nevertheless adequate precautions should be taken when the drug is used in patients with impaired cardiovascular systems.

The antiemetic action of 'Stelazine' may mask signs of overdosage of toxic drugs or may obscure the diagnosis of conditions such as intestinal obstruction and brain tumor.

Although 'Stelazine' has shown very little potentiating activity, caution should be observed when it is used in large doses in conjunction with sedatives or depressants.

CONTRAINDICATIONS

'Stelazine' is contraindicated in comatose or greatly depressed states due to central nervous system depressants.

AVAILABLE

Tablets, 1 mg. and 2 mg., in bottles of 50, 500 and 5000. (Each tablet contains 1 mg. or 2 mg. of trifluoperazine as the dihydrochloride.)

For psychiatric patients who are hospitalized or under close supervision:

Tablets, 5 mg. and 10 mg., in bottles of 50, 1500 and 5000. (Each tablet contains 5 mg. or 10 mg. of trifluoperazine as the dihydrochloride.)

Multiple-dose Vials, 10 cc. (2 mg./cc.), in boxes of 1 and 20. (Each cc. contains, in aqueous solution, 2 mg. of trifluoperazine as the dihydrochloride, 4.75 mg. of sodium tartrate, 11.6 mg. of sodium biphosphate, 0.3 mg. of sodium saccharin, and 0.75% of benzyl alcohol as preservative.)

Concentrate (for hospital use), 10 mg./cc., in 2 fl. oz. bottles, in cartons of 4 and 12. (Each cc. contains 10 mg. of trifluoperazine as the dihydrochloride.)

Prescribing information adopted July 1961

PARNATE®

brand of tranylcypromine

PRESCRIBING INFORMATION

The physician should be familiar with the material on dosage, side effects and cautions given below before prescribing 'Parnate', and with the principles of monoamine oxidase inhibitor therapy and the side effects of this class of drugs as reported in the literature. Also, the physician should be familiar with the symptomatology of mental depressions and alternative methods of treatment to aid in the careful selection of patients for 'Parnate' therapy.

INDICATIONS AND LIMITATIONS OF USE

'Parnate' is indicated for the relief of symptoms of mental depression which may include dejected mood, self-depreciation, lowered activity levels, difficulty in making decisions, disturbed eating and sleeping patterns, and variations of these basic symptoms as described in the literature. The therapeutic utility of monoamine oxidase inhibitors is limited specifically to depressive symptoms; these drugs may aggravate some co-existing symptoms such as agitation or anxiety.

In psychiatry, 'Parnate' is indicated in the following diagnostic categories, subject to the limitation stated above: reactive and other psychoneurotic depressions, involutional melancholia, depressive phase of manic-depressive psychosis, psychotic depressive reactions. In the psychiatric treatment of severe endogenous depressions, it is impossible to predict, with presently known data, which patients will respond best to 'Parnate' and which to ECT. 'Parnate' may be indicated in some reactive depressions in which ECT is not indicated. 'Parnate' is not recommended to treat essentially normal responses to temporary situational difficulties.

Note: In depressed patients, the possibility of suicide should always be considered and adequate precautions taken. Exclusive reliance on drug therapy to prevent suicidal attempts is unwarranted, as there may be a delay in the onset of therapeutic effect or an increase in anxiety and agitation. Also, of course, some patients fail to respond to drug therapy.

CLINICAL EXPERIENCE

Extensive clinical trials with 'Parnate' have confirmed its effectiveness and versatility. As always in the evaluation of drugs for psychic disorders, some variation in efficacy has been reported.

These studies provide the following data on the effectiveness and fundamental properties of 'Parnate':

1. In 500 patients on whom complete data are available for statistical analysis, marked or moderate improvement was reported in 77% of the nonpsychotic patients. Marked improvement was reported in 40% and moderate improvement in 27% of the psychotic patients. Some investigators have pointed out that improvement in certain instances, particularly in milder cases, may have been due to spontaneous remission of symptoms.
2. Improvement is seen within 48 hours to three weeks after starting 'Parnate'; the response can be accelerated by using higher than standard initial dosages.
3. 'Parnate' acts primarily as an antidepressant rather than as a euphoriant. Patients feel essentially normal on 'Parnate' therapy.
4. 'Parnate' can facilitate psychotherapy by increasing the patient's willingness to exert mental effort and reducing symptom-centered preoccupations.
5. 'Parnate' appears to prevent relapses in some patients who have been treated initially with ECT.

DOSAGE

Dosage should be adjusted to the requirements of the individual patient. Dosage increases should be made only in increments of 10 mg. per day and ordinarily at intervals of one to three weeks. Side effects occur more often as dosage is increased.

Reduction from peak to maintenance dosage may be desirable before withdrawal. If withdrawn prematurely, original symptoms will recur. No tendency to produce rebound depressions of greater intensity has been seen with 'Parnate', although this is a theoretical possibility in patients treated at high dosages. Experimental work indicates that inhibition of monoamine

oxidase persists for only a few days after withdrawal. Thus, any side effects due to this inhibition will probably recede rapidly upon withdrawal, which should be a distinct advantage of 'Parnate' therapy when the patient exhibits poor tolerance to antidepressant medication.

Because there is a striking relationship between dosage and speed of response, two dosage schedules are provided:

A. Standard dosage. (This schedule will not always produce prompt results, but it will hold the incidence of side effects to a minimum.)

1. Recommended starting dosage is 20 mg. per day – administered 10 mg. b.i.d. (morning and afternoon).
2. Continue this dosage for two to three weeks.
3. If no signs of a response appear, increase dosage to 30 mg. daily—20 mg. upon arising and 10 mg. in the afternoon.
4. Continue this dosage for at least a week.
5. As soon as a satisfactory response is obtained, dosage may usually be reduced to a maintenance level.
6. Some patients will be maintained on 20 mg. per day; many will need only 10 mg. daily.
7. If dosages above 30 mg. daily are desired for use in exceptionally resistant cases, refer to the schedule of intensive dosage.

B. Intensive dosage (for accelerated response). (This schedule is for use in hospitalized patients or those under comparable supervision whenever a prompt effect is more desirable than a relative absence of side effects.)

1. Recommended starting dosage is 30 mg. per day. Administer 20 mg. in the morning and 10 mg. in the afternoon.
2. Continue this dosage for one week.
3. If no signs of a response appear, increase dosage gradually at intervals of several days to one week.
4. Dosages above 60 mg. per day are not advisable.
5. As soon as a satisfactory response is obtained, dosage may usually be reduced gradually to a maintenance level.
6. Some patients may be maintained on 20 mg. per day; many will need only 10 mg. daily.

Note: When ECT is being administered concurrently, 10 mg. b.i.d. can usually be given during the series, then reduced to 10 mg. daily for maintenance therapy.

SIDE EFFECTS

A. At standard dosages. Side effects in patients treated with standard doses of 'Parnate' are qualitatively the same as seen at higher dosages but are generally less frequent and less severe.

The patient may experience restlessness, overstimulation, or insomnia; may notice some weakness, drowsiness, episodes of dizziness, or dry mouth; or may report nausea, diarrhea, abdominal pain, or constipation. Occasionally, headaches have occurred. Symptoms of postural hypotension have been seen most commonly, but not exclusively, in patients with pre-existent hypertension; blood pressure returns to pretreatment levels rapidly upon discontinuation of the drug. Other side effects which might occur in rare instances are tachycardia, urinary retention, significant anorexia, skin rashes, edema, palpitations, blurred vision, tinnitus, chills, paresthesia, muscle spasm and tremors, impotence, sweating and possibly paradoxical hypertension.

Most of these side effects can usually be relieved by lowering the dosage or by giving suitable concomitant medication.

B. At intensive treatment dosages. When 'Parnate' is used for intensive treatment to control symptoms more rapidly, an increase in the incidence and severity of side effects must be anticipated.

At doses above 30 mg. daily, postural hypotension is a major side effect of 'Parnate' therapy. It affects largely the systolic readings and occurs mainly, but not exclusively, in patients with a history of hypertension. Rare instances of syncope have been seen. Dosage increases should be made more gradually in patients showing a tendency toward hypotension at the starting dose. Postural hypotension can be relieved by having the patient lie down until blood pressure returns to normal.

Other side effects which may occur are listed above under *standard dosages*. Headaches have occasionally been severe and incapacitating. Overstimulated behavior, which may include increased anxiety, agitation and manic symptoms, can be evidence of either a side effect or an excessive therapeutic action; if this occurs, reduce dosage or administer a phenothiazine tranquilizer.

CAUTIONS

Extensive clinical and laboratory work has shown that there is little likelihood of blood or liver toxicity. Since 'Parnate' is a non-hydrazine compound, it should prove to be exempt from the toxic effects on the liver thought to be due to the hydrazine moiety of some other drugs. However, severe toxic reactions have occurred with some monoamine oxidase inhibitors. Pending further clinical experience, 'Parnate' should probably not be used in patients with a history of liver disease or in those with abnormal liver function tests. Drug-induced jaundice is often difficult to differentiate from other jaundice. However, there has been sufficient clinical experience with 'Parnate' to demonstrate that, if it has any potentiality for producing jaundice, the reaction must be rare. Also, the usual precautions should be observed in patients with impaired renal function since there is a possibility of accumulative effects in such patients.

Although 'Parnate' has been used in combination with various drugs (particularly Stelazine®, brand of trifluoperazine), some monoamine oxidase inhibitors have been reported to have marked potentiating effects on certain drugs, e.g., sympathomimetics, central nervous system depressants, hypotensive agents and alcohol. Therefore, the physician should bear in mind the possibility of a lowered margin of safety when 'Parnate' is combined with potent drugs and should adjust dosage carefully. 'Parnate' should not be used in combination with imipramine. (The reaction of a patient who attempted suicide with a deliberate overdosage of 'Parnate' and imipramine was more severe than would have been predicted from the properties of either drug.)

CASES REQUIRING SPECIAL CONSIDERATION

Administer with caution to patients with recent myocardial infarction or coronary artery disease with angina of effort. Increased physical activity and, more rarely, hypotension have been reported. The pharmacologic properties of 'Parnate' suggest that it may have a capacity to suppress anginal pain that would otherwise serve as a warning sign of myocardial ischemia. When 'Parnate', like any agent which lowers blood pressure, is withdrawn from patients who tend to be hypertensive, blood pressure may again rise to undesirable levels.

When 'Parnate' is combined with a phenothiazine derivative or other compound known to affect blood pressure, elderly patients and those with cardiovascular inadequacies should be observed more closely because of the possibility of additive hypotensive effects.

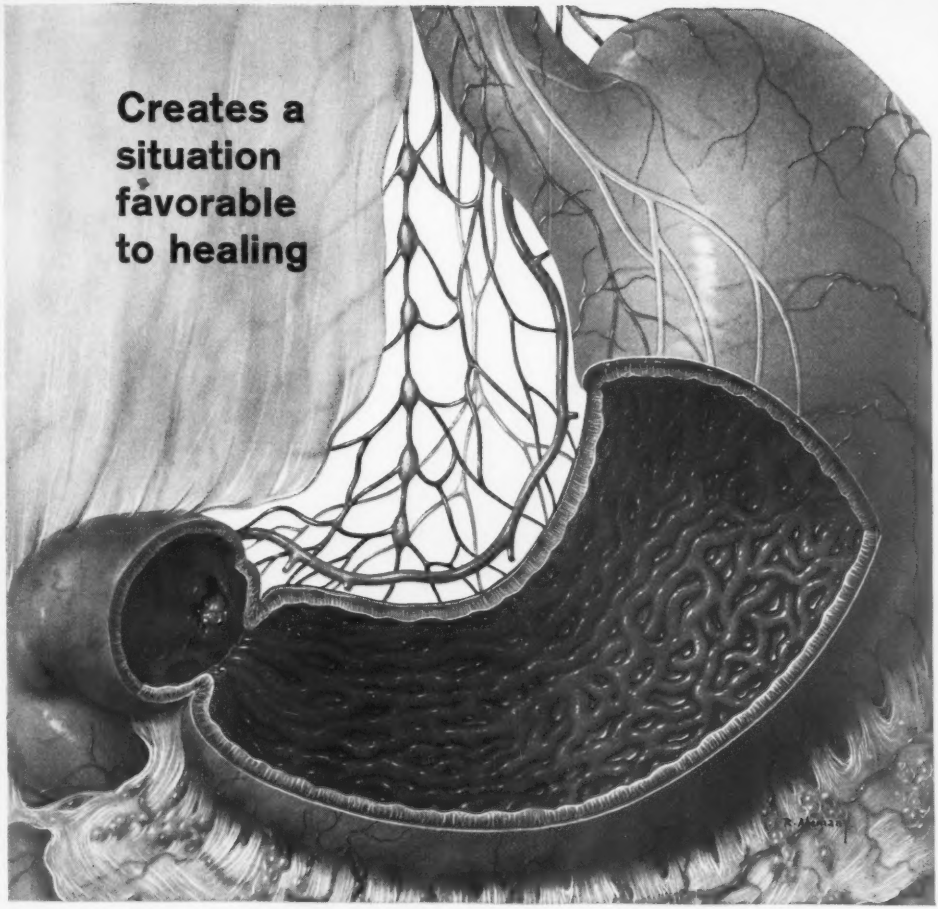
In patients being transferred to 'Parnate' from another monoamine oxidase inhibitor or from imipramine, allow a medication-free interval of one week, then initiate 'Parnate' using half the normal dosage for at least the first week of therapy. Similarly, a few days should elapse between the discontinuance of 'Parnate' and the administration of another monoamine oxidase inhibitor or of imipramine.

Because the influence of 'Parnate' on the convulsive threshold is variable in animal experiments, suitable precautions should be taken if epileptic patients are treated.

AVAILABLE

Tablets, 10 mg., in bottles of 50 and 1500. (Each tablet contains 10 mg. of tranylcypromine, as the sulfate.)

Prescribing information adopted Feb. 1961.



In ulcer: 'Combid' *Spansule* capsules provide emotional as well as physical control. 'Combid' reduces secretion, spasm and nausea—as well as anxiety, tension and apprehension—for 10 to 12 hours after just one capsule. A convenient q12h regimen provides 24-hour, continuous control; creates a situation favorable to healing.

SK&F

Combid® Spansule®

brand of sustained release capsules

'Combid' *Spansule* capsules are a logical combination of 5 mg. of Darbid® (brand of isopropamide) as the iodide, a unique, inherently long-acting anticholinergic, and 10 mg. of Compazine® (brand of prochlorperazine) as the dimaleate, the outstanding tranquilizer/antiemetic, in sustained release form.

Among the many conditions in which 'Combid' *Spansule* capsules are indicated are: peptic ulcer, hyperchlorhydria, pyloroduodenal irritability, irritable or spastic colon, gastric neurosis, gastritis, aerophagia, pyrosis, "nervous stomach," functional diarrhea, drug-induced diarrhea, mucous colitis, ulcerative colitis, genitourinary spasm, and nausea and vomiting of pregnancy.

DOSAGE: One 'Combid' *Spansule* capsule b.i.d. (every 12 hours). Some patients may require only one capsule every 24 hours, on arising. Only in the exceptional patient will it be necessary to increase the dosage to two capsules b.i.d. (morning and evening).

CAUTIONS AND CONTRAINDICATIONS: As is true with any preparation containing an anticholinergic, 'Combid' *Spansule* capsules should not be prescribed for patients with glaucoma, pyloric obstruction, or prostatic hypertrophy. Also, because of the antiemetic action of the 'Compazine' component (a phenothiazine derivative), 'Combid' *Spansule* capsules should not be used where nausea and vomiting are believed to be a manifestation of intestinal obstruction or brain tumor.

Clinical experience has demonstrated that 'Combid' has a wide margin of safety and that there is little likelihood of blood or liver toxicity or neuromuscular reactions (extrapyramidal symptoms). The physician should be aware, however, of their possible occurrence. When 'Combid' is used with depressant drugs, the possibility of an additive effect should be borne in mind. An occasional patient may experience mild drowsiness when first taking 'Combid'.

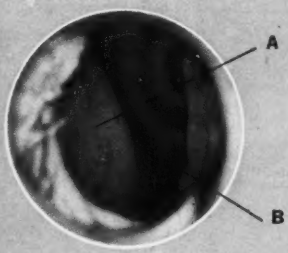
Prescribing information adopted January, 1961.

24-hour relief of running nose, sneezing and nasal stuffiness of "colds" with

ONE ORNADE® SPANSULE® q12h

brand of sustained release capsules

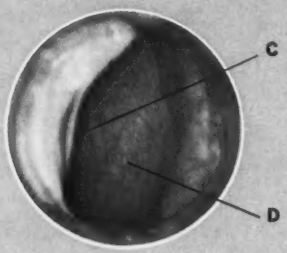
the unique oral nasal decongestant with a special drying agent



BEFORE TAKING 'ORNADE'

A—Note enlargement of turbinate, partially closing airway.

B—Septum is in deep shadow and is only partly visible since little light penetrates past swollen turbinate into nostril.



12 HOURS AFTER TAKING 'ORNADE'

C—Turbinate has shrunk to normal. Patency of airway, established by 2nd hour, is maintained into 12th hour.

D—A larger area of septum is visible and is clearly seen as more light penetrates to rear of nostril.

PRESCRIBING INFORMATION

The comprehensive formula of 'Ornade' *Spansule* capsules contains a special drying agent, isopropamide iodide, in addition to a decongestant and an antihistamine. Isopropamide iodide acts to reduce excessive weeping and nasal and paranasal secretions. The decongestant, phenylpropanolamine, reduces vascular engorgement and often permits blocked sinus cavities to drain. The antihistamine, 'Teldrin', reduces sneezing, rhinorrhea and itching of the eyes. Acting together, additively, these three agents combine to provide outstanding relief from upper respiratory distress.

FORMULA: Each 'Ornade' *Spansule* sustained release capsule contains 8 mg. of Teldrin® (brand of chlorpheniramine maleate) and 50 mg. of phenylpropanolamine hydrochloride, so prepared that a therapeutic dose is released promptly and the remaining medication, released gradually and without interruption, sustains the effect for 10 to 12 hours; and 2.5 mg. of isopropamide, as the iodide. Because isopropamide iodide is inherently long-acting, it has not been necessary to put it into sustained release form; therefore, the entire dose of isopropamide iodide is released upon ingestion.

INDICATIONS: 'Ornade' *Spansule* capsules are recommended for prompt and prolonged relief from respiratory tract congestion and hypersecretion associated with: the common cold, acute, subacute and chronic sinusitis, influenza, vasomotor rhinitis, postnasal drip, allergic rhinitis; hay fever, "rose fever," etc.

DOSAGE (adults and children over 6): For all-day, all-night relief, one 'Ornade' *Spansule* capsule q12h. When taken at bedtime, 'Ornade' keeps patients symptom-free throughout the night and usually enables them to wake up in the morning uncongested and with airways free.

SIDE EFFECTS: Drowsiness, "nervousness," or insomnia may occur on rare occasions, but are usually mild and transitory.

CAUTIONS AND CONTRAINDICATIONS: Use with caution in the presence of severe hypertension. 'Ornade' should not be used in patients with glaucoma or prostatic hypertrophy. NOTE: The iodine in isopropamide iodide may alter PBI test results and will suppress I^{131} uptake.

SUPPLIED: In bottles of 30 capsules.

Prescribing information adopted January, 1961.

SK&F *Smith Kline & French Laboratories*

consultant

December 1961

Included in this issue:

Mental Illness: Recognition and Referral
A Simple Method for Treating Stasis Ulcers
Ways to Improve Your Treatment of Adolescents

From SK&F—to help you in your practice

Medical Film Center—*one of the many services offered to physicians by SK&F*

More than thirty 16 mm. motion pictures with sound are available to you without charge from the SK&F Medical Film Center. They include postgraduate teaching films, films on the clinical use of SK&F products and documentaries for showing to lay groups. The SK&F film library also includes some exceptionally interesting films on mental health and psychiatry. Other SK&F services available to you include:

- SK&F Medical Color Television
- Special Resin No. 648 for the control of hyperkalemia in renal insufficiency
- Product overdosage information
- Mental Health Services.

For a copy of our medical film catalogue, supplies of our products, or information about other services, ask your SK&F representative, write Smith Kline & French Laboratories, 1500 Spring Garden Street, Philadelphia 1, Pa., or call us at LOcust 4-2400.

consultant

December 1961

CONSULTANT is published monthly by Smith Kline & French Laboratories for practicing physicians. Authors are chosen because of expert knowledge of their topics, and their participation does not imply endorsement of any of the products advertised. As a service to readers, the authors will answer questions pertaining to their topics; the most informative questions and answers will be published in later issues. CONSULTANT welcomes original manuscripts and suggestions for topics. Please address all correspondence, including questions for the authors, to CONSULTANT, Smith Kline & French Laboratories, 1500 Spring Garden St., Philadelphia 1, Pa.

CORRESPONDENCE

CONSULTANT welcomes questions and comments about any of the topics covered. The authors will answer all questions by mail, and some of the most informative replies will be published in this section (names will be withheld on request). Please address all correspondence to CONSULTANT, SK&F Laboratories, 1500 Spring Garden Street, Philadelphia 1, Pa.

Bad Breath from "Black Hairy Tongue"

(Consultant, October '61)

Dear Doctor Seltzer:

The condition of "black hairy tongue" associated with a decomposition odor in one of my patients had failed to respond to treatment. Is there an effective therapy for this distressing condition?

– Melvin Klein, M.D.
Coral Gables, Florida

The condition is rather rare, but is not considered serious. The "hairy" appearance is due to hypertrophied filiform papillae projecting from the dorsum of the tongue. No relationship is known to exist between this condition and cancer, or any disease, though it often occurs in people who have poor oral hygiene and who are heavy smokers or tobacco chewers. The papillae may become blackened by pigment from tobacco or coffee. Drugs have been suspected as causal agents, since hairy tongue has been known to occur in patients receiving antibiotics or phenothiazines, but since it also occurs in people not receiving drugs, this may be coincidental. The odor you mention undoubtedly comes from decomposition of food particles trapped in the papillae. The best solution to the problem is good oral hygiene. An effective measure is to scrub the area with a toothbrush dipped in hydrogen peroxide, and then rinse the mouth and gargle with a 50% solution of hydrogen peroxide. When very long, the papillae can be cut off with a pair of long-handled, curved scissors, but there may be bleeding if they are cut too close to the tongue.

– Albert P. Seltzer, M.D.

More about Pregnancy in Double Cervix and Uterus

(Consultant, October '61)

Dear Doctor Mengert:

I saw your letter to Dr. Kurth and thought you might be interested in two cases I have had.

Case 1 – Double vagina (septum), double uterine cervix (septum), complete with one corpus. Spontaneous labor at 8 months with dystocia from opposite cervix. A live baby was delivered by Cesarean section and the uterine septum was removed. A subsequent pregnancy was delivered at full term, again by Cesarean section.

Case 2 – Double cervix, double vagina – 5 or 6 spontaneous abortions at 2½ to 3 months. Septum removed from vagina; uterine septum removed at hysterotomy. Delivered a live baby one year later by Cesarean section.

I had not realized actually that this was as rare as it is. Incidentally, both women were Rh negative. Case two was AB negative.

– Dale R. South, Jr., M.D.
Troy, Ohio

Steroids for Acne

(Consultant, October '61)

Dear Doctor Sternberg:

You outline the use of steroids – then you say you do not advise this treatment for juvenile or ordinary pustular acne.

Would you tell me what treatment you would use for girls 12-14-16 years of age; would steroids disturb their menstrual cycle? Also discuss treatment for boys in the same age bracket. – W. B. Spalding, M.D.
Plattsburg, Missouri

The corticosteroid treatment, in our opinion, should be reserved for only the deep pustular and cystic acnes which are producing considerable scarring.

For the average moderate acne we recommend a combination treatment of good personal hygiene in cleaning the face, an astringent antiseptic acne lotion, usually one containing sulphur and a keratolytic, and so-called "acne surgery" in which blackheads are removed and small pustules are opened. – Thomas H. Sternberg, M.D.

An Orchid for CONSULTANT

Sir:

I would like to say that your small magazine CONSULTANT has impressed me immensely. Sometimes one cannot find all the information given in one of your issues in a whole month of the current medical literature elsewhere. And it pleases me that you are not trying to hide what you have to say behind a lot of unintelligible medical jargon.

– A. Fadul, M.D.
Gary, Indiana

Our thanks to Dr. Fadul for his encouraging words. – ED.

SURGERY

Carl Schiller, M.D.
State University of New York

Carl Schiller is Assistant Clinical Professor of Surgery at the State University of New York in Brooklyn. He is also Attending Surgeon in Charge of Plastic and Reconstructive Surgery at Coney Island Hospital and Maimonides Hospital in Brooklyn. Dr. Schiller received his medical degree at New York University School of Medicine and thereafter was appointed Archibald Fellow in Plastic and Reconstructive Surgery at McGill University. He is a member of the American Society of Plastic and Reconstructive Surgery and a Fellow of the American College of Surgeons.

FINGER-TIP TRAUMA

Treatment of finger-tip trauma is usually considered as minor surgery, but, if improperly done, may result in major disability. To help avoid such unfortunate results, I have gathered together the following tips on the treatment of finger-tip trauma.

Some General Rules

The best prophylaxis against infection is thorough, prolonged, and early cleansing of the skin with hexachlorophene soap followed by copious irrigation of the wound with saline. Devitalized tissue should be thoroughly excised. Antibiotics are needed only when the wound is badly contaminated or when circulation is endangered. However, if surgery must be delayed, antibiotics should be used to lengthen the "Golden Period" (6-10 hours after contamination before bacteria begin to multiply). To prevent the development of tetanus, a toxoid injection should be given as a booster. If the patient has not been actively immunized and tetanus infection seems likely, antitoxin should be used after skin testing.

Almost all procedures are carried out under local digital nerve block. I use a #25 needle, and enter the skin dorsally where it is thinnest and causes the least pain. One to 1½ cc. of 2% Xylocaine® are deposited on each side of the finger near the digital nerve as it lies beneath the thick skin just volar to the midlateral line (Figure 1). One-half cc. may be placed subcutaneously across the top to catch fibers innervating the dorsal aspect and sometimes, the nail. Never use adrenalin because it may cause digital spasm, which in turn may lead to gangrene